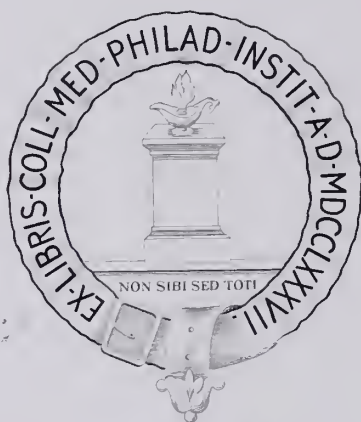


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Number 1

An Approach to Hypocalcemic Disorders in Children

JAMES E. HADDOW, M.D.*

It is unusual for the serum calcium level to be low in a child, and for that reason the physician confronted with such a problem may have difficulty in knowing how to proceed with further evaluation. The purpose of this article will be to review the several ways in which hypocalcemia may present and to suggest an approach which should allow for accurate diagnosis and treatment. Recent progress in the area of calcium metabolism has provided new diagnostic tests and a better understanding of hypocalcemic disorders, making it particularly worthwhile to consider this topic at the present time.

Initially, hypocalcemia may be discovered for several reasons: (1) A younger child may have convulsions prompting measurement of serum calcium levels as part of the seizure evaluation. (2) At any age the finding of carpal or pedal spasm would indicate the need for serum calcium levels. (3) Rickets, either clinically apparent or found by X-ray, might be associated with hypocalcemia. (4) As part of routine serum biochemical screening (such as SMA-12) a low serum calcium level might be discovered. (5) Hypocalcemia might be found in screening family members when an individual is known to have a calcium metabolic disorder. The two commonest symptoms of childhood hypocalcemia, seizures and carpopedal spasm, may go on for a considerable time before appropriate testing is done. Individuals with carpal spasm have been repeatedly dismissed from clinics and emergency facilities with the diagnosis of psychosomatic illness, and youngsters with recurrent grand mal seizures have occasionally been diagnosed as having hypocalcemia only after considerable time has elapsed.

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Seizure and carpopedal spasm resulting from hypocalcemia both are thought to occur because serum ionized calcium (and extracellular calcium) is necessary for the stability of biological membranes. An excess makes membranes too stable and unable to depolarize, while a deficiency makes membranes depolarize indiscriminately. This is particularly true for neuromuscular membranes and is responsible for the major symptomatology of hypocalcemia as well as electrocardiographic changes. Hypomagnesemia and alkalosis may also be responsible for such symptoms and membrane changes; magnesium through a mechanism similar to that of calcium and alkalosis because it causes increasing amounts of calcium to be bound to serum proteins, thus making it unavailable for membrane stability. For those reasons, serum magnesium levels, albumin and pH should also be determined when a suspected hypocalcemic disorder is first under investigation. It is also worth remembering that ionized calcium's capacity to suppress biological membrane excitability may produce nonspecific improvement when it is infused intravenously into a seizing patient. Such improvement cannot be used as proof that the patient is suffering from a hypocalcemic disorder.

Once hypocalcemia has been confirmed, one should consider the disorders listed in Table 1. The next studies to be done would include x-rays of knees and possibly of other bones to assess for metaphyseal dysplasia (rickets) or other bone pathology, serum phosphorus which would also help to narrow the field of diagnostic possibilities as indicated in the table, and alkaline phosphatase whose elevation would indicate increased osteoblastic activity.¹ In children the normal range of serum

TABLE I

<i>DISORDERS WITH RICKETS</i> Serum PTH Elevated Serum PO ₄ Low (except #3)	<i>HYPOPARATHYROIDISM</i> Serum PTH Low Serum PO ₄ Normal to High	<i>PSEUDOHYPOPARATHYROIDISM</i> Serum PTH Normal or High Serum PO ₄ Normal to High
1. Nutritional Deficiency of Vitamin D	1. Early Onset (first year)	1. End-Organ PTH Unresponsiveness
a) <i>low dietary intake</i>	a) <i>X-linked recessive</i>	a) <i>classical</i> (Albright) abnormal phenotype and PTH unresponsiveness of bone and kidney
b) <i>increased requirement</i> (anticonvulsive therapy)	b) <i>sporadic</i> both males and females absence thymus and parathyroids (Di George Syndrome)	b) <i>normal phenotype</i> kidneys unresponsive bones normally responsive
c) <i>malabsorption</i>	2. Later Onset	c) <i>hypomagnesemia</i> kidneys unresponsive (reversible)
2. Pseudodeficiency Rickets (Vitamin D dependent) hereditary defect in 1,25 (OH) ₂ D synthesis	a) <i>familial or sporadic</i> associated with moniliasis and Addison's Disease	
3. Renal Failure	3. Surgical Absence of Parathyroids	2. Biologically Ineffective Endogenous PTH
4. Hepatic Failure	4. Hypomagnesemia with Diminished PTH Secretion	a) end-organs normally responsive

phosphorus is higher than for adults, the values gradually approaching adult levels with advancing age.² The same is true for normal ranges of alkaline phosphatase.^{3,4} When labelling either value as normal or abnormal, it would be necessary first to consult tables of age-related normal values.

Table I also includes typical serum levels of immunoreactive parathyroid hormone for the three groups of disorders. It has only been possible to measure this hormone for the past several years and even now the assay is performed only in selected centers.⁵⁻⁹ In spite of this, it is possible to have such a determination done, and a generous sample of serum should be frozen at -20°C, and saved for this and other possible studies as soon as the investigation of hypocalcemia is underway.

As soon as results become available on serum phosphorus levels and x-rays of knees, it should be possible to narrow the diagnostic list. If rickets is found, then with rare exception both hypoparathyroidism and pseudohypoparathyroidism are excluded.¹⁰ A low serum phosphorus would lend further support, and the diagnostic possibilities listed as associated with rickets could then be considered. All possible diseases associated with hypocalcemia and rickets are also associated with secondary hyperparathyroidism. This is true because the unavailability of active vitamin D has produced a selective malabsorption of calcium from the gut and thus stimulated an outpouring of parathyroid hormone in an attempt to keep the serum calcium normal.^{11,12} This excess parathyroid hormone is also responsible for producing low serum phosphorus through increased renal phosphate excretion. Large amounts of parathyroid hormone also produce generalized aminoaciduria, which is a constant finding in the presence of hyperparathyroidism.¹³ The diag-

nostic possibilities for rickets can be narrowed rapidly — hepatic failure only produces rickets when far advanced, and renal failure also is associated with rickets only when far advanced. A decreased dietary intake of vitamin D could be evaluated by history as could chronic ingestion of anti-epileptic medication. Malabsorption should be apparent also during the history and physical examination. Pseudodeficiency rickets may be more difficult to diagnose but should be suspected once other hypocalcemic rachitic illnesses have been excluded. Pseudodeficiency rickets has recently been identified as a genetic disorder, inherited as an autosomal recessive characteristic, in which the enzyme for activating vitamin D in the kidney is missing. Normally, vitamin D ingested and absorbed, would first be hydroxylated in the liver and then in the kidney to produce 1,25 (OH)₂ D.¹⁴ This latter compound is the only active form of vitamin D, and individuals who are unable to manufacture it become rachitic rapidly. In cases where a question of vitamin D sufficiency is raised, there is now an assay for 250HD available,¹⁵ and some of the serum frozen earlier in the evaluation could be used for that purpose if necessary.

The treatment of rickets varies, depending upon which of the causes is found. Vitamin D deficiency rickets requires 2,000-5,000 units of vitamin D per day during the first month of therapy while bones are healing.¹³ With lower doses, there have been occasional instances where hypocalcemia was aggravated due to the rapid shifting of mineral into bone. Once healing is complete, vitamin D dosage may be lowered to the normal maintenance level of 400 units per day. An individual taking anticonvulsant medication will require up to 10 times the usual maintenance dose of vitamin D on a continuing

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently — both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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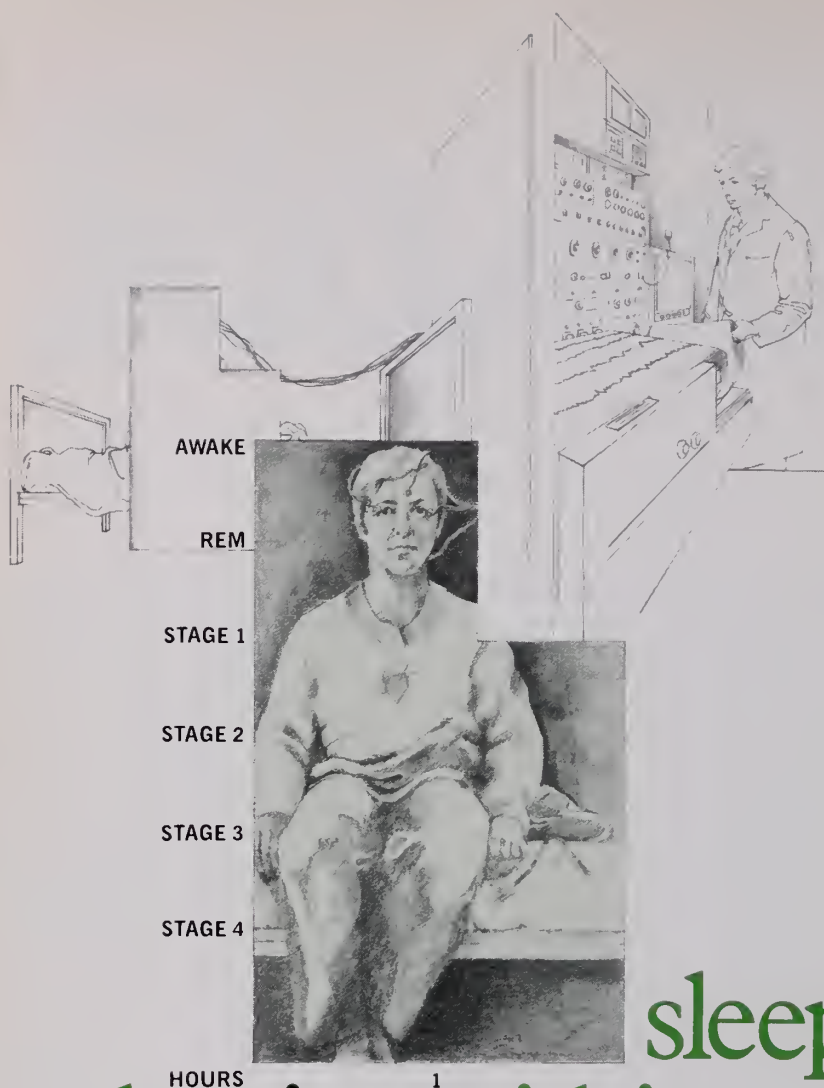
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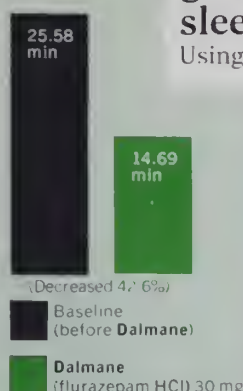


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Average Time Required
to Fall Asleep (4 Studies,
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confirmed by clinical studies in four geographically separated sleep research laboratories²⁻⁵

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Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening, in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

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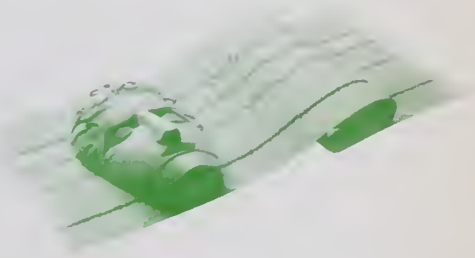
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Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 mL (2 mg.) t.i.d.; 5 to 8 years, 4 mL (2 mg.) q.i.d.; 8 to 12 years, 4 mL (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonsful (10 mL, 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 mL. A plastic dropper calibrated in increments of 1/2 mL (total capacity, 2 mL) accompanies each 2-oz. bottle of Lomotil liquid.

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basis. A patient with pseudodeficiency rickets will require either large doses of vitamin D (up to 50,000 units/day) or a small amount of dihydrotachysterol (Philips Roxanne), a synthetic form of vitamin D which does not require renal hydroxylation.

There are other rickets-producing diseases not listed in Table 1. Most such diseases produce rickets because of renal phosphate loss, and include such entities as familial hypophosphatemic rickets.¹⁷ In these cases, the unavailability of phosphorus stops normal metaphyseal bone crystal function in spite of the fact that calcium metabolism is completely normal. For this reason, these diseases are purposely excluded from the evaluation of hypocalcemia.

A hypocalcemic child without rickets would most probably suffer from some form of either hypoparathyroidism or pseudohypoparathyroidism. Table 1 summarizes the diagnostic possibilities listed under those two headings. One would expect to find a normal to high serum phosphorus in all such cases, but circulating parathyroid hormone would be low in association with hypoparathyroidism and elevated with pseudohypoparathyroidism. Even before results of parathyroid hormone levels become available, however, it should be possible to narrow down the diagnostic possibilities and in some cases actually make the diagnosis.

If parathyroid glands and thymus are congenitally absent as in the Di-George Syndrome,¹⁸ then immunologic incompetence would accompany the hypoparathyroid condition and give direction towards accurate diagnosis. A patient suffering from moniliasis as well as hypoparathyroidism also would be easily identifiable.¹⁹ Surgical absence of parathyroid glands should be a readily explainable cause as should be a hypomagnesemic state. On occasion, hypomagnesemia results in suppression of parathyroid function, a condition which can be immediately reversed by magnesium repletion.^{20,21} Thus, a significant number of cases of hypoparathyroidism carry with them a clinical marker to aid in diagnosis.

When pseudohypoparathyroidism is the cause of hypocalcemia, there may also be accompanying physical or biochemical stigmata to help make rapid identification possible. Until recently only the classical form of pseudohypoparathyroidism was known. That condition is associated with short metacarpals, short stature, obesity, and mental retardation and can be readily diagnosed on clinical grounds.²²⁻²⁷ Hypomagnesemia^{28,29} has also been recently shown on occasion to suppress end-organ responsiveness to adequate circulating parathyroid hormone (also reversible with magnesium repletion).

The remaining disorders listed under hypoparathyroidism and pseudohypoparathyroidism would require at least that serum parathyroid hormone

levels be known before further attempts could be made towards diagnosis. A low measurement would point towards hypoparathyroidism, while an elevated value would indicate one of the recently recognized forms of pseudohypoparathyroidism.³⁰⁻³³

These latter conditions have been better understood since the availability of urinary cyclic AMP responses to intravenously administered exogenous parathyroid hormone.³⁴ Using this diagnostic test, it has been possible to define examples of both end-organ unresponsiveness to parathyroid hormone and biologically ineffective endogenous parathyroid hormone as causes of pseudohypoparathyroidism in phenotypically normal individuals.

Depending upon the final diagnosis, genetic counselling might be indicated, since some of the inheritable disorders produce serious disease. Treatment of all hypoparathyroid and pseudohypoparathyroid disorders would be directed towards raising serum calcium to safe levels, and some form of vitamin D would be the treatment of choice. Such treatment would require careful adjustment of dose; especially in the first weeks of therapy to avoid vitamin D toxicity, and frequent serum calcium and phosphorus measurements would be necessary.

Because of their relative infrequency, childhood disorders of calcium metabolism may provide the clinician with difficulty in recognition, diagnosis, and management. It is possible most of the time to reach a satisfactory conclusion using the guidelines presented in this paper, and in many cases subsequent therapy produces gratifying results.

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Is Hemoglobin-Oxygen Affinity Relevant?

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Life depends on the ability of flowing blood to carry oxygen from the lungs to the tissues. The usual approach to the treatment of conditions associated with limited oxygen delivery involves measures to increase blood flow by increasing vessel caliber. More recently, as a result of increased research into the physical and biochemical characteristics of the erythrocyte, it appears increasingly probable that important clinical benefits may be derived from biochemical modifications of the oxygen-carrying properties of the red cell itself. Although various methods are currently available to alter the fluid properties of whole blood on the one hand and the efficiency of hemoglobin to carry oxygen on the other, definitive experiments to establish the physiologic effects and therapeutic practicalities of such modifications have yet to be carried out.

The remarkable effectiveness of hemoglobin as a vehicle for oxygen is due primarily to its ability to combine reversibly with roughly 65 times the volume of oxygen that would otherwise be transported by simple solution in the plasma.¹ Adding to this efficiency is the ability of the molecule to undergo changes in its affinity for oxygen which enhance the uptake or release of oxygen in response to changing biochemical environments within the body. These differences in hemoglobin-oxygen kinetics can be explained, at least in part, by conformational shifts of the four component globin chains which influence the binding of oxygen by their associated heme groups.² It is also characteristic of hemoglobin that as its heme groups become successively oxygenated, the affinity for oxygen of the remaining, unoxygenated hemes increases greatly.³ This property is reflected in the sigmoidal shape of the oxyhemoglobin dissociation curve which relates oxygen saturation on the ordinate to partial pressure (PO_2) on the abscissa. The physiologic superiority of the shape of this curve in comparison to a more linear relationship is evidenced by the relatively larger amount of oxygen exchanged per mm Hg PO_2 difference at partial pressures associated with the release of oxygen in the peripheral microcirculation (30-50 mm Hg).

The affinity of hemoglobin for oxygen is also affected by a number of ligands which bind the globin chains in various ways and thus restrict their move-

ments. These include the hydrogen ion, carbon dioxide, and intraerythrocytic organic phosphates, particularly 2,3-diphosphoglycerate (2,3-DPG).^{4,5} By limiting the access of oxygen to hemoglobin, these compounds reduce the volumes of the gas taken up at all levels of PO_2 , with the result that the oxyhemoglobin dissociation curve is shifted to the right without changing its overall shape. Because hydrogen ions and carbon dioxide are both normal products of metabolism, their concentrations increase in peripheral capillaries but diminish as carbon dioxide is excreted in the lungs. In theory, resulting shifts in hemoglobin-oxygen affinity would be expected to favor both the release of oxygen to the tissues and its uptake in the pulmonary capillaries. By the same token, since the intraerythrocytic concentration of 2,3-DPG increases in response to hypoxia, it is commonly assumed that oxygen delivery is appropriately enhanced in diseases characterized by limited oxygen supply.⁶⁻⁸ The fact remains, however, that the effect of hemoglobin-oxygen affinity on tissue oxygen delivery has not yet been defined, primarily because of the lack of methods to quantify oxygen concentrations at the tissue levels, but also because of the difficulty in separating, *in vivo*, the relative influences of biochemical and hemodynamic events.

Although a vast number of studies have associated a wide variety of physiologic and pathologic conditions with shifts in hemoglobin-oxygen affinity (for excellent reviews see⁹⁻¹³), investigators have not been able to demonstrate consistent changes in the efficiency of oxygen delivery in humans or animal models in which oxygen affinity has been deliberately shifted. Valeri and Collins,¹⁴ for example, observed no effect on systemic oxygen consumption or cardiac output in eight patients who received up to 2500 ml of low 2,3-DPG donor blood. Woodson, Wranne, and Detter¹⁵ found that the work performance of rats was relatively unaffected by exchange transfusions which resulted in a marked decrease in hemoglobin-oxygen affinity. Recently, Riggs, Shafer, and Guenter¹⁶ have reported no change in oxygen consumption or cardiac output in Rhesus monkeys in which oxygen affinity was increased by similar means. Working with rabbits in which hemoglobin-oxygen affinity was altered chronically and acutely, our group^{17,18} has shown (a) that compensatory cardiac output responses overcome changes in the ability of blood to deliver oxygen, and, (b) that under hypoxic conditions, neither high nor low oxygen affinity improved tissue oxygen availability, as measured with chronically implanted polarographic

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tissue oxygen electrodes.

Demonstration of the effect of hemoglobin-oxygen affinity on oxygen transport in the intact animal may also be made difficult by the wide range of oxygen pressures at which oxygen is delivered in various organs. It is important to realize that a rightward shift of the oxyhemoglobin dissociation curve will enhance the delivery of oxygen only from relatively saturated blood; that is, along the upper shoulder of the oxyhemoglobin dissociation curve. When hypoxia causes oxygen transport to take place on the straight mid-portion of the curve, the relative position of the curve has little or no effect upon oxygen delivery, since affinity has little effect on the slope at this level. Below 35 mm Hg PO_2 , however, oxygen will be released more readily by a *left* shifted curve, at least down to the point at which the PO_2 gradient between capillary plasma and the site of mitochondrial oxygen utilization becomes critically small. Of particular interest in this regard is a very recent report by Eaton, Skelton, and Berger demonstrating significantly greater survival from altitude hypoxia by rats pre-treated with cyanate to increase hemoglobin-oxygen affinity.¹⁹ From these relationships, it is evident that the ease with which oxygen is released from hemoglobin will vary from organ to organ and within specific organs. As a result, interpretations regarding the respiratory functions of blood as well as approaches for the biochemical modifications of hemoglobin-oxygen affinity for therapeutic reasons will be different at different levels of arterial PO_2 .

Clearly, further studies of the physiologic role of hemoglobin-oxygen affinity must focus on individual tissues. As an experimental model, the isolated, beating heart is particularly appropriate because of the broad scope of physiologic information this preparation provides, because cardiac tissue extracts more oxygen from a given volume of blood over a greater PO_2 range than any other tissue in the body, and particularly because of the therapeutic implications which would derive from new information regarding oxygen delivery to the ischemic myocardium. It is well known that under normal conditions, oxygen delivery to the heart is primarily a function of coronary blood flow which in turn is regulated by vasomotor control. When flow is obstructed by atheromatous plaques, or when the amount of oxygen in the arterial blood is limited for any reason, the coronary vessels are maximally dilated and further oxygen delivery cannot be achieved through local hemodynamic means. Under these circumstances an ability to enhance release of oxygen from hemoglobin through biochemical modifications would have enormous therapeutic applications in the treatment of myocardial infarction, which remains the single most frequent cause of death in this nation.

The role of hemoglobin-oxygen affinity in myo-

cardial oxygen delivery has attracted considerable attention, both as a possible factor in the cause of angina pectoris and myocardial infarction occurring in the absence of coronary vascular disease, and because acute and unexplained changes in affinity have been observed in patients suffering from myocardial ischemia. Since the development of coronary cineangiography in the mid-1960's, several reports have appeared describing angina and infarction in individuals with patent coronary vessels.²²⁻²⁹ It is estimated that nine percent of all patients with angina have normal coronary vessels.²³ While some workers have found no abnormalities in hemoglobin-oxygen affinity in this condition,²⁸ others have observed a distinct rightward shift.^{22,26,27} Despite the theoretical enhancement of oxygen delivery such a shift would imply, data has been presented suggesting the rate of red cell oxygen release is actually retarded in these patients.^{27,29}

More recently, a small but statistically significant decrease in hemoglobin-oxygen affinity has been observed to occur in blood perfusing the hearts of patients in whom angina pectoris was induced by atrial pacing.³⁰ In another study, approximately 30 percent of 103 patients with coronary disease demonstrated a fall in the oxygen affinity of coronary sinus blood during pacing.³¹ These findings could not be explained on the basis of changes in intracellular or plasma pH, 2,3-DPG, or ATP. Within the last year, Kostuk and co-workers³² have demonstrated considerably larger rightward shifts (4 mm Hg) in samples of both venous and arterial blood from patients with myocardial infarctions, and they have correlated the degree of shift with the clinical severity of the individual case. Again no associations could be made with respect to the usual modifiers of hemoglobin-oxygen affinity.

It appears established, then, that myocardial ischemia may be accompanied by a rightward shift of the oxyhemoglobin dissociation curve which frequently is unassociated with measurable changes in the familiar hemoglobin ligands. The possibility arises that this shift results from factors related to the hypoxic myocardium itself, and further, that these factors may alter aspects of red cell oxygen transport other than hemoglobin-oxygen affinity, such as red cell membrane diffusivity and deformability. Indeed, recent work by our group³³ has demonstrated that important discrepancies may be noted between the rate of oxygen transport, as predicted by the oxyhemoglobin dissociation curve, and the rate as actually measured in blood flowing through a laboratory capillary model. This information is of particular interest in the light of a report by Guy, *et al.*,³⁴ who described impaired oxygen release by red cells from patients with myocardial ischemia, a right-shifted curve, and normal coronary arteries. Apparently, evaluation of oxygen delivery in the face of myocardial ischemia must include measure-

ments of cell deformability and membrane oxygen permeability as well as hemoglobin oxygen kinetics.

Although the shifting affinity of hemoglobin for oxygen has been recognized for several decades, and has been assigned an important role in the theory of oxygen transport by blood, demonstration of its influence on tissue oxygen delivery in vivo has been hindered by compensatory changes in blood flow. As the supply of blood to a given tissue is restricted, however, oxygen delivery to that tissue becomes increasingly a function of hemoglobin-oxygen affinity. Where oxygen reserves are minimal, as in the myocardium, the position of the oxy-hemoglobin dissociation curve may well be a critical factor in the survival of the tissue, and thus the entire organism. If such a relationship can be shown to exist, the development of a biochemical method to alter hemoglobin-oxygen affinity may provide an important lifesaving therapy.

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In Vitro Screening Tests of Thyroid Function

A Review

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INTRODUCTION

Hyper and hypothyroidism are clinical states which have both obvious and subtle manifestations affecting many different organ systems. Consequently, a question of abnormal thyroid function is frequently entertained in the differential diagnosis of many medical problems and a final decision concerning the state of thyroid compensation is commonly dependent upon confirmation of the clinical picture by laboratory tests.

There have been significant advances in the understanding of thyroid function over the past ten to fifteen years, and more direct and specific methods for the evaluation of clinical problems of thyroid compensation have been extended to the clinician. It is the intention of this review to discuss the basic in vitro screening tests which are readily available today for the assessment of thyroid homeostasis and to indicate the advantages and disadvantages of each test.

PROTEIN BOUND IODINE (PBI)/BUTANOL EXTRACTABLE IODINE (BEI)

These two tests are mentioned only to emphasize that they are no longer of any significant value as a method of evaluating thyroid function and have been replaced by direct measurement of serum thyroid hormone levels. These PBI and BEI methods are dependent upon the measurement of iodine and are not direct assessments of the level of circulating thyroid hormone.¹ They are frequently made completely unreliable by the common use of iodine containing contrast materials used in radiologic infusion studies and by intentional or unwitting ingestion of excessive amounts of iodine in the diet. In addition, such common hospital and office practices as swabbing areas of skin with iodine containing disinfectants result in absorption of large quantities of inorganic iodine through the skin and will again prevent any useful interpretation of the level of iodine in the serum as a reflection of thyroid function.

TOTAL SERUM THYROXINE LEVEL (TOTAL T4)

Today it is possible to directly measure the amount of total circulating thyroxine (T4) independently of the iodine content of the blood. This is done by taking advantage of the fact that thyroid

binding globulin (TBG), the normal circulating plasma protein which has specific and high affinity for T4, can be used to specifically measure the total amount of thyroxine (T4) present in serum (Murphy-Pattee method).² The methodology for this test is well established, readily available, and no more expensive than that required for doing PBI's. Again, this method is in no way dependent upon serum iodine levels and is devoid of the limitations imposed by iodine dependent methods.

FREE SERUM THYROXINE LEVEL (FREE T4)

More than ninety-nine percent of thyroid hormone present in normal serum circulates bound to serum proteins, and in particular to thyroid binding globulin.³ A very small fraction of the total amount of T4 circulates unbound or "free." Although this amount of "free T4" is quantitatively very small, it is presently felt that this represents essentially the entire amount of T4 which is metabolically active.⁴

The "free T4" exists in a dynamic equilibrium with the much larger portion of T4 which is bound to TBG. Using the same principles of competitive protein binding as used to measure the total T4, but with certain modifications, it is possible to directly, accurately and reproducibly measure the amount of T4 that is present in the "free" or unbound state in serum.⁵ Frequently, it is most helpful to know the value of the free T4 since this is the metabolically active component and there are a number of circumstances which raise or lower the total amount of T4 that circulates bound to TBG to abnormal levels without significantly altering the concentration of the unbound or free T4. For example, pregnancy or the use of estrogen containing compounds will increase the amount of TBG and thereby bind more T4 in the serum and raise the total T4 level.⁶ The concentration of free T4 in these circumstances, however, remains within the normal range and the patient is euthyroid. Conversely, congenital deficiency of TBG, loss of TBG in the urine in nephrosis, iatrogenically induced decrease in TBG (eg: androgen therapy), or the use of drugs which displace T4 from TBG (eg: Dilantin®) can cause the total T4 level to fall while the unbound (free) T4 level remains essentially unchanged and the patient remains euthyroid. With true hyperthyroidism an elevation of the total T4 is accompanied by a rise of the free T4 out of the normal range and in hypothyroidism a fall of the total T4 is associated

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with a coincident decrease in the free T4 to subnormal levels.

Thus, it is evident that the total T4 may not infrequently be misleading as an index of a given patient's state of thyroid compensation unless coupled with measurement of the free T4 as well. Assessment of both total T4 and free T4 together gives a more reliable screen of a patient's basic thyroid status.

RESIN T3 UPTAKE (T3 UPTAKE)

This test probably causes more confusion for physicians than any other test used in evaluating thyroid function, and the concern that it evokes is in general entirely out of proportion to the clinical value of the test. This type of test gives an estimate of the relative binding capacity of a given patient's serum for a small amount of radioactive hormone added to the serum *in vitro*.⁷ The avidity of the serum being tested is an indirect indication of the amount of thyroid hormone which is circulating in the free state. In hyperthyroidism, the excess free thyroid hormone present in serum will compete with the added radioactive hormone and prevent it from binding to TBG. In hypothyroidism, the relative insufficiency of circulating free thyroid hormone will result in an increased binding of the added radioactive material to TBG in the patient's serum. When any material is added (eg: charcoal or a resin compound) which will pick up the radioactive hormone not bound to TBG and then is separated and counted for radioactivity, it is evident that the amount of resin-associated radioactivity from a hyperthyroid serum sample will tend to be greater than normal and that from a hypothyroid patient less than normal. Thus, hyperthyroidism tends to be associated with a high percentage resin uptake and hypothyroidism with a low uptake.

However, this indirect method of evaluating thyroid hormone economy is not particularly sensitive and patients with clinically evident hyper or hypothyroidism not infrequently have T3 uptake values that are still within the normal range. Also, excessive or subnormal amounts of TBG in the serum may result in abnormal T3 uptake tests and yet the patient can be completely euthyroid. Therefore, given the increasing availability of accurate measurements of total T4 and free T4 levels, this combination allows the physician a much more direct and sensitive evaluation of the patient's thyroid homeostasis than does reliance on resin-T3-uptake tests or other equivalents.

SERUM TSH

It has been well known for many years that the activity of the thyroid gland is regulated by secretion of a polypeptide hormone from the pituitary gland.⁸ This hormone is called thyroid stimulating hormone (TSH). Serum thyroid hormone and TSH

concentrations are both regulated according to a negative feedback mechanism where declining levels of thyroid hormone are sensed by the hypothalamic-pituitary axis which then induces an increased output of TSH by the pituitary gland. The TSH then causes increased synthesis and release of thyroid hormone from the normal thyroid gland and the resulting rise of thyroid hormone levels is sensed by the hypothalamus and pituitary gland and the TSH secretion is then decreased.

In people with normal thyroid glands and normal hypothalamic-pituitary function, this negative feedback system operates within rather closely maintained ranges. If, however, for some reason the thyroid gland is damaged (eg: Hashimoto's thyroiditis) and cannot maintain a normal output of thyroid hormone, the TSH output will increase above normal levels in an attempt to drive the thyroid harder and increase its productivity. Consequently, primary thyroid gland failure is characterized by a high serum TSH, and an elevated TSH level is now accepted as the *sine qua non* for the diagnosis of hypothyroidism due to thyroid gland failure.^{9,10}

It is now possible to accurately measure the level of TSH in human serum by means of radioimmunoassay, and this has proved to be one of the most significant advances in the evaluation of thyroid function in many years.^{9,10} Classic hypothyroidism is usually recognized clinically with a minimum of substantiating laboratory tests required to secure the diagnosis. However, most hypothyroidism encountered by the physician is not of an extreme nature. Rather, it is well recognized that less severe but definitely significant levels of primary hypothyroidism are frequently associated with subtle and nonspecific manifestations affecting many organ systems. It is also not unusual for the physician to be confronted with equivocal borderline low values for serum total T4 and free T4, and an accurate assessment of a given patient's thyroid status on clinical and laboratory grounds can be difficult to make. It is in this setting that the ability to measure TSH assumes great value since an elevation of the TSH above normal confirms the diagnosis of primary hypothyroidism and is a definite factor in resolving the question of whether or not a patient is hypothyroid.

Measurement of serum TSH is also of significant value in cases of clinically overt hypothyroidism. Although not needed for diagnostic purposes in obvious hypothyroidism, it has become a very valuable tool in the management of thyroid hormone replacement therapy. Previously, recognition of the point at which a particular hypothyroid patient had reached maximal compensation during a course of replacement thyroid hormone therapy was not always easy to assess. With the advent of the TSH assay, it is possible to follow the fall of the serum TSH level as replacement therapy is instituted and

when the TSH has been returned to the normal range the replacement dosage should be considered adequate. Using such criteria it has been demonstrated that the dosages of desiccated thyroid (three grains) and Synthroid® (0.3 mg) which had previously been estimated to be the average amount required to achieve euthyroidism were somewhat excessive and a dose of two to two and a half grains desiccated thyroid and 0.2 to 0.25 mg. Synthroid are more accurate average doses. However, in any given patient the exact dose required can be quite variable and the serum TSH level allows this dose to be defined on an individual basis.

Finally, the TSH level is of great value in discriminating between hypothyroidism of thyroid gland origin (primary) and that due to pituitary failure (secondary). With thyroid gland failure, the TSH will be high and with pituitary failure, TSH will be low or absent. This distinction is of more than academic value. Simple replacement of thyroxine alone is all that is required to correct primary hypothyroidism, but administration of thyroxine by itself in secondary (pituitary) hypothyroidism can be hazardous. Pituitary insufficiency is not a frequent cause of hypothyroidism, but when hypothyroidism does occur as a result of deficient TSH secretion by the pituitary, it is in almost every case a part of the picture of panhypopituitarism. Consequently, some degree of adrenal insufficiency due to lack of adrenocorticotrophic hormone is usually also present. Thus, thyroid hormone replacement therapy begun without coincident cortisol replacement may precipitate acute adrenal insufficiency as the metabolic demands of the body increase in the absence of adequate adrenal reserve. Therefore, whenever there is a question of pituitary incompetence in the face of hypothyroidism, a serum TSH level should be drawn and thyroxine replacement treatment should be accompanied by adequate glucocorticoid coverage until the results

of the TSH assay are reported, and the etiology of the hypothyroidism is defined.

In thyrotoxicosis, measurement of the serum TSH level is rarely of value since essentially all hyperthyroidism is the result of primary overactivity of the thyroid gland and pituitary TSH output is suppressed and TSH is unmeasurable in the serum. It is only after therapy has been instituted (eg: radioiodine, sub-total thyroidectomy) and the hyperthyroidism corrected that the TSH level becomes important. Since a significant portion of patients following radioiodine therapy or subtotal thyroidectomy will go on to become hypothyroid, an elevation of the serum TSH level is the most sensitive means of detecting early thyroid failure and is an indication for institution of replacement therapy.

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AN APPROACH TO HYPOCALCEMIC DISORDERS IN CHILDREN — *Continued from Page 4*

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The Hairless, Odorless Axilla: An Example of Selective End-Organ Unresponsiveness to Androgen

JAMES E. HADDOW, M.D.* and D. GRANT GALL, M.D.**

A family has come to our attention in which females over five generations have failed to develop axillary hair or axillary perspiration at puberty. This trait was transmitted silently from the first to the third generations through a male according to available historical information. The inheritance pattern is consistent with either X-linked dominance or autosomal dominance expressed only in females, and either of these possible modes of transmission is uncommon.¹

REPORT OF CASES

Case V-6. The proband was referred for evaluation of short stature at age 15 years. She had always been considered small for her age but grew at a constant rate below the third percentile. At age 9 years, she developed pyelonephritis and was discovered to have a hypoplastic left kidney. Subsequently, over the next five years, she had four more urinary tract infections. She also suffered from a right facial paralysis, dating from birth. Pubarche and thelarche at age 11 were followed by menarche one year later. At the time of examination, she had regular menses but stated that she had never developed axillary hair nor axillary perspiration, although perspiration was normal elsewhere both in volume and odor. Family history brought to light a number of female members in five generations with similar axillary findings (Figure 1). Many of the family members of both sexes were of short stature, but there was no history of renal disease. Only the index case, a sister, and her mother were available for physical examination. Remaining information was obtained historically from the mother.

On examination she was found to be of normal intelligence, with a height of 142 cm. and weight of 34 kg., both below the third percentile for her chronologic age.

Her skin was normal and displayed fine hair. Scalp and pubic hair were normal in texture, quantity and distribution. Axillary hair was absent, and no perspiration was visible although the room was very warm. Breasts and external genitalia were normal. Mild right facial paralysis and left scoliosis were present. Teeth and nails were normal.

The following laboratory results were normal: complete blood count, urinalysis, electrolytes, creatinine, blood urea nitrogen, urine amino acids, and 17-ketosteroids (8.1 mg/24 hours). Intravenous pyelogram demonstrated a left hypoplastic kidney and a normal right kidney. Bone age was 17 years.

Case IV-5. The mother of the proband was age 35, gravida 4, para 4, and had always been in good health except for mild hypertension. She had never perspired in the axillae nor had axillary hair ever appeared. Puberty was otherwise normal. Examination demonstrated a healthy female with a blood pressure of 150/90 who had a few strands of fine axillary hair. Laboratory

PEDIGREE OF THE F FAMILY

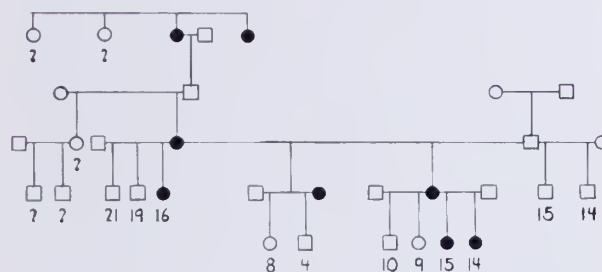


Fig. 1. Pedigree of the F family. Males are represented by open squares, unaffected females by open circles, and affected females by black circles. ? indicates members with no available information. Numbers in fourth and fifth generations indicate age in years.

studies revealed normal urine amino acids and 17-ketosteroids (6.5 mg/24 hours).

Case V-5. This 14-year-old sister of the index case was completely well. Puberty occurred at age 11 with normal breast development, pubic hair, and menstrual cycle. Axillary hair and perspiration were absent. Physical examination confirmed the history. Urinary amino acids were normal and 17-ketosteroids measured 7.6 mg/24 hours.

No other family members were available for study, and further studies were not carried out due to the family's reluctance.

DISCUSSION

The family tree for five generations is drawn out in Figure 1. Of interest is the fact that all females in the five generations about whom information is available (with the exception of two prepubertal females in the fifth generation) have the trait. No male in any generation is affected, and this is particularly significant in the second generation where the unaffected male apparently transmits the characteristic to at least one of his two daughters. Unfortunately, this individual was not available for examination. The tree further reveals that the proband's grandmother married twice and produced affected daughters by both marriages. The inheritance pattern is thus suggestive of either an autosomal dominant mode of transmission or of X-linked dominant transmission, in either case producing expression only in the female.

Growth of axillary and pubic hair in females is

Continued on Page 25

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The Relevance of Alpha-Fetoprotein Measurements in Prenatal Diagnosis

JAMES E. HADDOW, M.D. and ROBERT F. RITCHIE, M.D.*

During the past two years, convincing evidence has accumulated to show that amniotic fluid alpha-fetoprotein (AFP) levels are elevated when a fetus is affected by spina bifida or anencephaly.¹⁻⁶ The predictive accuracy of such measurements approaches 90 percent when an affected fetus suffers from anencephaly and 60 percent if spina bifida alone is present. Furthermore, abnormal AFP levels can, in most cases, be clearly shown at 16 weeks gestation, thus allowing the option of therapeutic abortion. Confirmation of neural tube anomalies may at times be obtained through X-ray or ultrasound techniques, but there are instances where alpha-fetoprotein levels themselves represent the single most reliable indicator. Since the procedure of amniocentesis carries a significant albeit not high risk, collection of amniotic fluid is not applicable as a screening procedure in the population-at-large. There is, however, a group of high-risk individuals who have already delivered a fetus with anencephaly or spina bifida,^{7,8} and such women may be subjected to amniocentesis for AFP measurement because there is a high degree of probability that they will produce a second affected offspring. In such cases, amniocentesis has already gained wide acceptance and can be considered a reliable clinical procedure.

More recently Brock, in England, has reported elevated maternal serum AFP levels as well as elevated amniotic fluid AFP levels early in the second trimester when fetuses have had neural tube defects.⁹⁻¹¹ If this report can be confirmed, then it is possible that entire populations of pregnant women may be tested for these defects. The availability of such a blood test for prenatal diagnosis would be unprecedented and would represent a significant advance in that area. Neural tube defects represent the commonest central nervous system anomalies, occurring at the rate of 8 per 1,000 live births in the United Kingdom, and at the approximate rate of 3.5 per 1,000 live births^{12,13} in southern New England. If the New England area figures for prevalence of neural tube anomalies are compared with those for phenylketonuria, the ratio would be 35:1, thus yielding a much greater number of affected fetuses diagnosed in a given screening program. If maternal serum AFP levels are proven reliable, the labora-

tory method necessary for delivering accurate results will require much attention, since it must measure quantities of serum AFP in the nanogram range.

In considering AFP's role in fetal diagnosis, it is worthwhile to review some of its unique characteristics. It is an alpha-1 globulin synthesized by fetal liver and yolk sac, may be produced as early as the sixth week of fetal life, and reaches peak concentrations of approximately 300mg/100ml in fetal serum at 13 weeks gestation.¹⁴⁻¹⁸ Thereafter, it falls steadily so that newborns ordinarily have levels of 10mg/100ml. Following delivery, serum AFP concentrations fall rapidly and adult levels of 2-17 nanograms/ml¹⁹ are reached by a few months of life. It is thought that the elevated amniotic fluid and maternal serum AFP levels which occur with spina bifida and anencephaly are present because of protein leakage from exposed fetal neural membrane surfaces. Even in the absence of fetal neural tube anomalies, amniotic fluid contains relatively large amounts of AFP,¹ and maternal serum shows definite increases over the non-pregnant population.²⁰ Normal ranges for AFP concentrations in both serum and amniotic fluid vary depending upon length of gestation, and normal values must be carefully defined before any actual diagnostic efforts can begin. Fetal urine is the major normal contributor to such levels since it contains as much as 48,000 nanograms/ml during the second trimester with concentration falling rapidly to nearly undetectable quantities in the third trimester.¹

Before its recognition as a useful test for prenatal diagnosis, alpha-fetoprotein was measured to help detect hepatoma and embryonal cell carcinoma.²¹⁻²³ Both of these tumors produce large quantities of AFP, and serum levels may be as high as in the fetus. With the development of more refined techniques, it also became possible to show that AFP serum levels became normal after successful tumor therapy and began to rise again as tumor recurred, thus making such measurements helpful in tumor therapy as well as diagnosis. The availability of more refined techniques also led to the discovery that serum alpha-fetoprotein concentrations were significantly elevated with hepatitis; never, however, being as high as in malignancy. Table 1 summarizes the sensitivity of currently available methods. Radioimmunoassay, the most sensitive and recently developed technique, has allowed for the

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TABLE I
METHOD FOR MEASURING AFP
LOWER LIMIT OF SENSITIVITY

	mg%	mcg/ml	nanog/ml
Immunoelectrophoresis	5	50	50,000
Micro-Ouchterlony	1	10	10,000
Electroimmunodiffusion	1	10	10,000
Immunoelectroosmophoresis	0.3	3	3,000
Single radial immunodiffusion	0.3	3	3,000
Radioimmunodiffusion	0.03	0.3	300
Radioimmunoassay	.000015	.015	15.6

more refined observations both in tumor and in prenatal diagnosis.

As experience with prenatal AFP measurements has broadened, other congenital problems have also been found in association with elevated values. In one instance, high levels of AFP in amniotic fluid predicted a case of congenital nephrosis.¹ High levels in another pregnancy were associated with a case of esophageal atresia.²¹ Twin pregnancies have produced measurements in the high normal to borderline abnormal range as has fetal distress.²⁵ It is likely that other such examples will come to light with time. For that reason, it is necessary to make use of diagnostic techniques such as X-ray and ultrasound for further information once alpha-fetoprotein levels have been found to be elevated.

At present it is possible in Maine to arrange for amniotic fluid AFP analysis in high risk pregnancies through the genetics counselling clinic at the Maine Medical Center. In addition, we are in the process of setting up and standardizing a radioimmunoassay method suitable for measuring serum concentrations of alpha-fetoprotein. After normal AFP values have been established for various stages of pregnancy, a pilot project will be undertaken to test the validity of such measurements in diagnosing fetal neural tube defects. If successful, the test will be made available for routine prenatal screening in Maine.

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Gonorrhea

Recommended Treatment Schedules – 1974

Physicians are cautioned to use no less than the recommended dosages of antibiotics.

UNCOMPLICATED GONOCOCCAL INFECTIONS IN MEN AND WOMEN

Drug Regimen of Choice:

Aqueous procaine penicillin G (APPG), 4.8 million units intramuscularly, divided into at least two doses and injected at different sites at one visit, together with one gram of probenecid, by mouth, just before the injections.

Alternative Regimens:

- A. Patients in whom oral therapy is preferred: Ampicillin, 3.5 gm, by mouth, together with one gram probenecid by mouth, administered at the same time. There is evidence that this regimen may be slightly less effective than the recommended APPG regimen.
- B. Patients who are allergic to the penicillins (penicillin G, ampicillin) or probenecid*:
 1. Tetracycline hydrochloride, 1.5 gm initially by mouth, followed by 0.5 gm by mouth four times per day for 4 days (total dosage, 9.5 gm). Other tetracyclines are not more effective than tetracycline hydrochloride. All tetracyclines are ineffective as single-dose therapy.
 2. Spectinomycin hydrochloride, 2.0 gm intramuscularly, in one injection.

Treatment of Sexual Partners:

Men and women with known recent exposure to gonorrhea should receive the same treatment as individuals known to have gonorrhea. Male sex partners of persons with gonococcal infection must be examined and treated because of the high prevalence of nonsymptomatic urethral gonococcal infection in such men.

Followup:

Followup urethral and other appropriate cultures should be obtained from men, and cervical, anal and other appropriate cultures should be obtained from women, 7 to 14 days after completion of treatment.

United States Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, Bureau of State Services, Venereal Disease Control Division, Atlanta, Georgia.

*Allergy to penicillin, ampicillin, probenecid, or previous anaphylactic reaction.

Treatment Failures:

Most recurrent infection after treatment with the recommended schedules is due to reinfection. True treatment failure after therapy with penicillin, ampicillin or tetracycline should be treated with 2.0 gm of spectinomycin intramuscularly.

Postgonococcal Urethritis:

Tetracycline, 0.5 gm, four times daily by mouth, for at least 7 days.

Pharyngeal Infection:

Pharyngeal gonococcal infections may be more difficult to treat than anogenital gonorrhea. Post-treatment cultures are essential followup for pharyngeal infection. The schedules of ampicillin and spectinomycin recommended for anogenital gonorrhea are ineffective in pharyngeal gonorrhea. Patients with pharyngeal gonorrhea whose infection is not eradicated after treatment with 4.8 million units of APPG plus one gram of probenecid, may be treated with 9.5 gm of tetracycline in the dosage schedule outlined above (Alternative Regimens).

Syphilis:

All patients with gonorrhea should have a serologic test for syphilis at the time of diagnosis. Seronegative patients without clinical signs of syphilis, who are receiving the recommended parenteral penicillin schedule, need not have followup serologic tests for syphilis. Patients treated with ampicillin, spectinomycin, or tetracycline should have a followup serologic test for syphilis after 3 months to detect untreated syphilis.

Patients with gonorrhea who also have syphilis should be given additional treatment appropriate to the stage of syphilis.

Not Recommended:

Although long-acting forms of penicillin (such as benzathine penicillin G) are effective in syphilotherapy, they have NO place in the treatment of gonorrhea. Oral penicillin preparations such as penicillin V are not recommended for the treatment of gonococcal infection.

TREATMENT OF UNCOMPLICATED GONORRHEA IN PREGNANT PATIENTS

- A. For women who are not allergic to penicillin:

Use the regimens of aqueous procaine penicillin G plus probenecid, or use ampicillin plus probenecid, as defined above.

B. Pregnant patients who are allergic to penicillins (there are several possible alternative regimens, each of which has potential disadvantages):

1. Erythromycin, 1.5 gm orally, followed by 0.5 gm four times a day for 4 days, for a total of 9.5 gm. This regimen is safe for mother and fetus, but efficacy has not been established. Erythromycin estolate should not be used in patients with underlying liver disease.
2. Cefazolin, 2 gm intramuscularly, with 1.0 gm of probenecid. Because of the possibility of cross-allergenicity between penicillins and cephalosporins, this regimen should not be used in a patient with a history of penicillin anaphylaxis.
3. Spectinomycin, 2 gm intramuscularly. This is an effective dose, but safety for the fetus has not been established.

Contraindicated:

Tetracycline should not be used for uncomplicated gonococcal infection in pregnancy because of potential toxic effects for mother and fetus.

ACUTE SALPINGITIS (PELVIC INFLAMMATORY DISEASE)

The diagnosis of acute salpingitis should be considered in women with acute lower abdominal pain and adnexal tenderness on pelvic examination. Since there are no completely reliable clinical criteria on which to distinguish gonococcal from nongonococcal salpingitis, endocervical cultures for *N. gonorrhoeae* are essential in such patients. Therapy, however, should be initiated immediately, without waiting for the results of the cultures.

A. Hospitalization: Hospitalization should be strongly considered for women with suspected salpingitis in these situations:

1. Uncertain diagnosis, where surgical emergencies must be excluded.
2. Suspicion of pelvic abscess.
3. Pregnant patients with salpingitis.
4. Inability of the patient to follow an outpatient regimen of oral medication, especially because of nausea and vomiting.
5. Failure to respond to outpatient therapy.

B. Antimicrobial Agents: Controlled studies of the treatment of acute salpingitis are not available. Initial management must *AT LEAST* be adequate for gonococcal salpingitis. These regimens are known to be adequate for the treatment of gonococcal salpingitis:

1. Outpatients:

- a. 1.5 gm tetracycline hydrochloride, given as a single oral loading dose, followed by 500 mg, taken orally, four times daily for 10 days.
- b. Aqueous procaine penicillin G (APPG), 4.8 million units intramuscularly, divided into at least two doses and injected at different sites at one visit, *OR* 3.5 gm of oral ampicillin. One gram of oral probenecid is given along with either penicillin or ampicillin, and both are followed by 500 mg of ampicillin, taken orally, four times daily for 10 days.

2. Hospitalized patients:

- a. Aqueous crystalline penicillin G, 20 million units, given intravenously each day until clear-cut improvement occurs, followed by 500 mg of ampicillin taken orally four times daily, to complete 10 days of therapy. The need for additional or alternative antibiotics for the treatment of nongonococcal salpingitis requires further study. Since it is impossible to distinguish gonococcal from nongonococcal salpingitis clinically, many physicians also use an aminoglycoside in addition to penicillin and/or antibiotics which are effective against *Bacteroides fragilis* as initial therapy.
- b. Tetracycline hydrochloride, 500 mg, given intravenously four times daily until improvement occurs, followed by 500 mg taken orally four times daily, to complete 10 days of therapy. This regimen should not be used for pregnant women or for patients with renal failure.

3. Failure to improve on the recommended regimens does not necessarily indicate the need for stepwise additional antibiotics, but requires reassessment of the possibility of other diagnoses and of the specific microbial etiology.

C. The effect of the removal of an intrauterine device on the response of acute salpingitis to antimicrobial therapy and on the risk of recurrent salpingitis requires further study.

D. Adequate treatment of women with acute gonococcal salpingitis must include examination and appropriate treatment of their male sex partners because of the high prevalence of nonsymptomatic urethral gonococcal infection in such men. Failure to treat male sex partners is a major cause of recurrent gonococcal salpingitis.

E. Followup of patients with acute salpingitis is essential. All patients should receive repeat pelvic examinations and cultures for *N. gonorrhoeae* after treatment.

DISSEMINATED GONOCOCCAL INFECTION

- A. Equally effective treatment schedules in the arthritis-dermatitis syndrome include:
1. Aqueous crystalline penicillin G, 10 million units intravenously per day for 3 days, or until there is significant clinical improvement. This may be followed with ampicillin, 500 mg four times a day orally, to complete 7 days of antibiotic treatment.
 2. Ampicillin, 3.5 gm orally, plus probenecid, 1.0 gm, followed by ampicillin, 500 mg four times per day orally, for at least 7 days.
- B. In penicillin and/or probenecid allergic patients:
1. Tetracycline, 1.5 gm orally, followed by 500 mg four times a day orally, for at least 7 days. Tetracycline should not be used for complicated gonococcal infection in pregnancy because of potential toxic effects for mother and fetus.
 2. Erythromycin, 0.5 gm intravenously every 6 hours, for at least 3 days.
- C. Additional measures:
1. Hospitalization is indicated in patients who are unreliable, have uncertain diagnosis, or have purulent joint effusions or other complications.
 2. Immobilization of the affected joint(s) appears helpful. Repeated aspirations and saline irrigations appear beneficial, but controlled studies of these procedures have not been performed. Open drainage of joints other than the hip is now generally discouraged in patients with gonococcal arthritis.
 3. Intra-articular administration of penicillin is unnecessary, since penicillin levels in the synovial fluid of inflamed joints approximate serum levels; furthermore, intra-articular injection per se may produce a toxic synovitis.
- D. Meningitis and endocarditis due to the gonococcus require high-dose intravenous penicillin therapy (at least 10 million units per day) for longer periods: usually at least 10 days for meningitis and 3-4 weeks for endocarditis.

GONOCOCCAL INFECTION IN PEDIATRIC PATIENTS

Pediatric patients encompass those from birth to adolescence. When a child is post-pubertal and/or weighs over 100 pounds, he or she should be treated with dosage regimens as defined above for adults.

WITH GONOCOCCAL INFECTION IN CHILDREN, THE POSSIBILITY OF CHILD ABUSE MUST BE CONSIDERED!

The efficacy of therapeutic regimens for uncomplicated and complicated gonococcal infections of childhood is unproven at present.

Prevention of Neonatal Infection:

All pregnant women should have endocervical cultures examined for gonococci as an integral part of prenatal care.

Prevention of Gonococcal Ophthalmia:

- A. One percent silver nitrate (do not irrigate with saline, as this may reduce efficacy).
- B. Ophthalmic ointments containing tetracycline, erythromycin, or neomycin are also probably effective.
- C. **NOT RECOMMENDED:** Bacitracin ointment (not effective) and penicillin drops (sensitizing).

Management of Infants Born to Mothers With Gonococcal Infection:

Orogastric and rectal cultures should be taken from all patients. Blood cultures should be taken if septicemia is suspected. Aqueous crystalline penicillin G, 50,000 units/kg/day, should be administered in two daily doses intravenously, if cultures or Gram-stained smears reveal gonococci. The duration of therapy should be determined by clinical response. In suspected septicemia, an aminoglycoside should also be administered.

Neonatal Disease:

- A. Gonococcal ophthalmia: Patient should be hospitalized. Antimicrobial agents: Aqueous crystalline penicillin G, 50,000 units/kg/day, in two or three doses intravenously for 7 days, **PLUS** frequent saline irrigations and instillation of penicillin, tetracycline or chloramphenicol eyedrops.
- B. Complicated infection: Arthritis and septicemia should be treated by hospitalization and administration of aqueous crystalline penicillin G, 75,000-100,000 units/kg/day, in four doses, or procaine penicillin G, 75,000-100,000 units/kg/day, in two doses, for 7 days. Meningitis should be treated with aqueous crystalline penicillin G, 100,000 units/kg/day, divided into two or three daily intravenous doses and continued for at least 10 days.

Childhood Disease:

Gonococcal ophthalmia should be treated with hospitalization and by the administration of aqueous crystalline penicillin G intravenously, 75,000-100,000 units/kg/day, in four doses, or procaine penicillin G, intramuscularly, 75,000-100,000 units/kg/day, in two doses, for 7 days, **PLUS** saline irrigations and instillation of penicillin, tetracycline or chloramphenicol eyedrops. Topical antibiotics *alone* are **NOT** recommended in therapy of gonococcal ophthalmitis. The source of the infection must be identified.

Uncomplicated vulvovaginitis and urethritis

usually do not require hospitalization. Both may be treated at one visit with aqueous procaine penicillin G, 75,000-100,000 units/kg intramuscularly, and probenecid, 25 mg/kg by mouth. Topical and systemic estrogen therapy are of no benefit in vulvovaginitis. All patients should have followup cultures, and the source of infection should be identified, examined and treated.

Infection complicated by peritonitis or arthritis should be treated by hospitalization and administration of aqueous crystalline penicillin G, intravenously, 75,000-100,000 units/kg/day, in four doses, or procaine penicillin G, 75,000-100,000 units/kg/day intramuscularly, in two doses for 7

days.

Treatment of patients with allergy to penicillin: Patients under 6 years of age should be treated with erythromycin, 40 mg/kg/day, in four doses by mouth, for 7 days, for uncomplicated disease. Complicated disease should be treated with cephalothin, 60-80 mg/kg/day in four doses intravenously, for 7 days. Patients older than 6 may be treated with an oral regimen of tetracycline, 25 mg/kg, as an initial dose, followed by 40-60 mg/kg/day in four doses, for 7 days, or an intravenous regimen consisting of tetracycline, 15-20 mg/kg/day, in four doses, for 7 days.

The Board of Directors of the Pine Tree Organization invites all physicians licensed to practice in Maine to join the organization. A membership application follows. Please complete it and forward it to Pine Tree Organization for Professional Standards Review, Inc. c/o Richard T. Chamberlin, M.D., President, P.O. Box 706, 99 Western Avenue, Augusta, Maine 04330.

PINE TREE ORGANIZATION FOR PROFESSIONAL STANDARDS REVIEW, INC.

MEMBERSHIP APPLICATION

I, _____, presently admitted to practice medicine in the State of Maine, hereby apply for membership in the Pine Tree Organization for Professional Standards Review, Inc.

I understand that there are no financial commitments (i.e. dues) as a condition to my membership and that my membership shall continue as long as I am licensed to practice medicine in the State of Maine or until I voluntarily elect to resign. Resignation may be made at any time in writing directed to the Clerk of Pine Tree Organization for Professional Standards Review, Inc.

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Clinically Important Drug Interactions

RUSSELL R. MILLER, Pharm.D., Ph.D.

The following table includes drug interactions which have been shown to be clinically significant in man. It does *not* include: (1) interactions that have been demonstrated only in laboratory animals, (2) familiar additive or synergistic interactions (e.g. alcohol and chloral hydrate), (3) well-known antagonistic interactions (e.g. alcohol and disulfiram), and (4) most interactions between foods and drugs (e.g. delayed absorption and onset of action of pentobarbital when taken after eating).

The table is organized by drug categories; the categorization is the same as that used in the American Hospital Formulary Service. Below each category title, in the column labeled "Drug A" are listed individual drugs or groups of drugs which interact with those drugs listed in the "Drug B" column.

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Unwanted effects which may occur as a result of an interaction are briefly described in the third column. The probable mechanism of the interactions is given in the fourth column. The last column provides documentation. As a convenience for those who may want to read further, most of the citations refer to two well documented drug interaction manuals instead of several hundred original publications. These manuals are: (1) the American Pharmaceutical Association's *Evaluations of Drug Interactions* (and its supplement) and (2) P. D. Hansten's *Drug Interactions*. These are the most useful reference books on the subject; they probably should be made available wherever questions on drug interactions frequently arise.

With the exception of interactions between drugs in the same category, all interactions are listed twice in the table. Thus, information on the interaction between azathioprine and allopurinol can be found under both azathioprine (in the category "Antineoplastic Agents") and allopurinol (in the category "Agents Used in Gout").

Drug categories are listed in the table in the same order as they are listed in the American Hospital Formulary Service.

The decision to include or not to include an interaction in the table was an arbitrary judgment in some cases. Thus, the table should not be considered a complete compilation.

CLINICALLY IMPORTANT DRUG INTERACTIONS

Drug A	Drug B	Adverse Effect	Probable Mechanism	Reference
Antibiotics (8:12)				
Aminoglycoside antibiotics ¹	Ethacrynic acid (Edecrin)	Ototoxicity	Additive	A-93
Amphotericin B (Fungizone)	Digitalis glycosides	Digitalis toxicity	Hypokalemia	H-110
Cephalosporins	Gentamicin	Nephrotoxicity	Unknown	H-116
	Probenecid	Increased cephalosporin toxicity	Inhibition of renal excretion	H-115
Cephaloridine (Loridine)	Furosemide (Lasix)	Nephrotoxicity	Unknown	H-116
Chloramphenicol	Oral anticoagulants	Increased anticoagulant effect	Inhibition of microsomal enzyme activity	H-22
	Diphenylhydantoin (Dilantin)	Diphenylhydantoin toxicity	Inhibition of microsomal enzyme activity	H-56
	Tolbutamide (Orinase) and Chlorpropamide (Diabinese)	Enhanced hypoglycemic effect	Inhibition of microsomal enzyme activity	AS-399 A-28
	Barbiturates	Decreased serum level of griseofulvin	Unknown	A-68
Griseofulvin	Oral anticoagulants	Decreased anticoagulant effect	Unknown	A-163
Lincomycin (Lincocin)	Kaolin (Kaopectate)	Decreased serum level of lincomycin	Absorption of lincomycin	A-98

CLINICALLY IMPORTANT DRUG INTERACTIONS

<i>Drug A</i>	<i>Drug B</i>	<i>Adverse Effect</i>	<i>Probable Mechanism</i>	<i>Reference</i>
Neomycin	Oral anticoagulants	Increased anticoagulant effect	Unknown	H-28
Tetracyclines	Antacids containing calcium, magnesium, or aluminum	Decreased serum level of tetracyclines	Formation of non-absorbable complexes	A-136
	Dairy products	Decreased serum level of tetracyclines	Formation of non-absorbable complexes	A-136
	Iron preparations (oral)	Decreased serum level of tetracyclines	Formation of non-absorbable complexes	AS-397
	Sodium bicarbonate	Decreased serum level of tetracyclines	Unknown	H-148
Doxycycline (Vibramycin)	Barbiturates	Decreased serum level of doxycycline	Induction of microsomal enzyme activity	Ref. 1
	Carbamazepine (Tegretol) and Diphenylhydantoin (Dilantin)	Decreased serum level of doxycycline	Induction of microsomal enzyme activity	Ref. 2
<i>Antibiotics (8:12)</i>				
Tetracycline	Oral anticoagulants	Increased anticoagulant effect	Unknown	H-32
Antibiotics that depress neuromuscular transmission ²	Methoxyflurane (Penthrane)	Nephrotoxicity	Unknown	A-138
	Anesthetics that depress neuromuscular transmission ³	Respiratory arrest or prolonged neuromuscular blockade	Synergistic effects on neuromuscular transmission	A-61
	Ether and curariform drugs ⁴	Respiratory arrest or prolonged neuromuscular blockade	Synergistic effects on neuromuscular transmission	A-65; A-111
<i>Antituberculous Agents (8:16)</i>				
Aminosalicylic Acid (PAS)	Probenecid	PAS toxicity due to increased blood levels	Inhibition of renal excretion	H-114
Isoniazid	Diphenylhydantoin (Dilantin)	Diphenylhydantoin toxicity	Inhibition of microsomal enzyme activity	A-51
	Antacids	Decreased serum level of isoniazid	Delayed and depressed absorption	Ref. 3
Rifampin	Oral anticoagulants	Decreased anticoagulant effect	Induction of microsomal enzyme activity	Ref. 4 Ref. 5
<i>Sulfonamides (8:24)</i>				
Sulfaphenazole (Sulfabid) Sulfisoxazole (Gantrisin)	Sulfonylurea antidiabetic agents ⁵	Enhanced hypoglycemic effect	Unknown	A-147
<i>Nitrofurans (8:36)</i>				
Furazolidone (Furoxone)	Sympathomimetic amines ⁶	Hypertensive crisis	Abrupt release of accumulated norepinephrine	A-12
Nitrofurantoin (Furadantin, Macrodantin)	Probenecid	Decreased efficacy of nitrofurantoin	Inhibition of renal tubular secretion	A-114
<i>Antineoplastic Agents (10:00)</i>				
Azathioprine (Imuran) and Mercaptopurine (Purinethol)	Allopurinol (Zyloprim)	Increased toxicity of antineoplastic agents	Inhibition of xanthine oxidase by allopurinol	A-105
Methotrexate	Salicylates	Increased serum level of free methotrexate	Displacement of methotrexate from binding sites	H-162
<i>Antiparkinsonism Agents (12:00)</i>				
Levodopa	Pyridoxine	Decreased antiparkinson effect	Increased decarboxylation of levodopa peripherally	A-96
	Monoamine oxidase inhibitors ⁷	Hypertensive crisis	Abrupt release of accumulated norepinephrine	A-95
	Tricyclic antidepressants ⁸	Decreased antiparkinson effect	Impaired absorption	In press
<i>Adrenergic Agents (12:12)</i>				
Amphetamine and related drugs ⁹	Guanethidine (Ismelin)	Decreased hypotensive effect	Displacement of guanethidine from site of action	A-70 A-75
	Reserpine	Reduced pressor effects of adrenergic drugs	Reserpine pretreatment depletes norepinephrine	A-57
Adrenergic drugs that act mainly by releasing norepinephrine ¹⁰				
	Sympathomimetic amines ⁶	Monoamine oxidase inhibitors ⁷	Hypertensive crisis	Abrupt release of accumulated norepinephrine
	Furazolidone (Furoxone)	Hypertensive crisis	Abrupt release of accumulated norepinephrine	A-20 AS-366

CLINICALLY IMPORTANT DRUG INTERACTIONS

<i>Drug A</i>	<i>Drug B</i>	<i>Adverse Effect</i>	<i>Probable Mechanism</i>	<i>Reference</i>
	Cyclopropane and halogenated hydrocarbon anesthetics ¹¹	Arrhythmias	Sensitization of heart to catecholamines	A-59 A-76
<i>Iron Preparations</i> (20:04.04)				
All oral preparations	Magnesium trisilicate	Reduced response to iron therapy	Impaired absorption of ferrous sulfate	H-232
	Tetracyclines	Decreased serum level of tetracyclines	Formation of non-absorbable complexes	AS-397
<i>Anticoagulants</i> (20:12.04)				
All oral agents	Aspirin	Increased anticoagulant effect	Additive	A-155
	Barbiturates	Decreased anticoagulant effect	Induction of microsomal enzyme activity	A-168
	Chloral Hydrate	Transient increase in anticoagulant effect	Displacement of anticoagulant from binding sites	A-157 Ref. 6
	Chloramphenicol	Increased anticoagulant effect	Unknown	H-22
	Cholestyramine (Cuemid, Questran)	Decreased anticoagulant effect	Binding in gastrointestinal tract	Ref. 7
	Clofibrate (Atromid-S)	Increased anticoagulant effect	Displacement of anticoagulant from binding sites	AS-405
	C-17-alkylated androgens ¹²	Increased anticoagulant effect	Unknown	A-166
	Disulfiram (Antabuse)	Increased anticoagulant effect	Inhibition of microsomal enzyme activity	H-24
	Ethchlorvynol (Placidyl)	Decreased anticoagulant effect	Induction of microsomal enzyme activity	H-39
	Glutethimide (Doriden)	Decreased anticoagulant effect	Induction of microsomal enzyme activity	A-162
	Griseofulvin	Decreased anticoagulant effect	Unknown	A-163
	Neomycin	Increased anticoagulant effect	Unknown	H-28
	Oxyphenbutazone (Oxalid, Tandearil)	Increased anticoagulant effect	Displacement of anticoagulant from binding sites	A-171
	Phenylbutazone (Azolid, Butazolidin)	Increased anticoagulant effect	Displacement of anticoagulant from binding sites	A-171
	Quinidine and quinine	Increased anticoagulant effect	Additive	A-173
	Rifampin	Decreased anticoagulant effect	Induction of microsomal enzyme activity	Ref. 4 Ref. 5
	Tetracycline	Increased anticoagulant effect	Unknown	H-32
	Thyroid hormones	Increased anticoagulant effect	Unknown	A-174
Dicumarol	Diphenylhydantoin	Diphenylhydantoin toxicity	Competition for same metabolic degradation site	H-55
	Sulfonylurea antidiabetic agents ⁵	Enhanced hypoglycemic effect	Inhibition of microsomal enzyme activity	H-73
<i>Digitalis Glycosides</i> (24:04)				
All preparations	Amphotericin B (Fungizone)	Digitalis toxicity	Hypokalemia	H-110
	Diuretics (causing potassium loss)	Digitalis toxicity	Hypokalemia	A-38
Digitoxin	Reserpine	Arrhythmias	Unknown	A-42
	Barbiturates	Decreased serum level of digitoxin	Induction of microsomal enzyme activity	H-224
	Cholestyramine (Cuemid, Questran)	Decreased serum level of digitoxin	Binding in gastrointestinal tract	H-225
<i>Antiarrhythmic Agents</i> (24:04)				
Propranolol (Inderal)	Antidiabetic agents	Enhanced hypoglycemic effect	Impairment of counterregulation	AS-378

CLINICALLY IMPORTANT DRUG INTERACTIONS

<i>Drug A</i>	<i>Drug B</i>	<i>Adverse Effect</i>	<i>Probable Mechanism</i>	<i>Reference</i>
Quinidine	Oral anticoagulants	Increased anticoagulant effect	Additive	A-173
	Reserpine	Increased antiarrhythmic effects and toxicity of quinidine	Additive when both drugs are initially given at same time	A-130
Quinidine or procainamide given postoperatively	Tubocurarine (Tubarine)	Recurarization	Additive	A-152
<i>Hypocholesterolemic Agents (24:06)</i>				
Cholestyramine (Cuemid, Questran)	Digitoxin	Decreased serum level of digitoxin	Binding in gastrointestinal tract	H-225
	Thyroid hormones	Reduced response to thyroid	Binding in gastrointestinal tract	A-143
	Cholestyramine (Cuemid, Questran)	Decreased anticoagulant effect	Binding in gastrointestinal tract	Ref. 7
Clofibrate (Atromid-S)	Oral anticoagulants	Increased anticoagulant effect	Displacement of anticoagulants from binding sites	AS-405
<i>Antihypertensive Agents (24:08)</i>				
Guanethidine (Ismelin)	Alcohol	Hypotension	Additive	AS-373
	Amphetamine and related drugs ⁹	Decreased hypotensive effect	Displacement of guanethidine from site of action	A-70 A-75
	Chlorpromazine	Decreased hypotensive effect	Displacement of guanethidine from site of action	Ref. 8
	Tricyclic antidepressants ⁸	Decreased hypotensive effect	Inhibition of uptake of guanethidine into adrenergic neurons	A-71
Reserpine	Digitalis	Arrhythmias	Unknown	A-42
	Quinidine	Arrhythmias	Additive	A-130
	Adrenergic drugs that act mainly by releasing norepinephrine ¹⁰	Reduced pressor effects of adrenergic drugs	Reserpine pretreatment depletes norepinephrine	A-57
<i>General Anesthetics and Muscle Relaxants (28:04)</i>				
Cyclopropane and halogenated hydrocarbon anesthetics	Sympathomimetic amines ⁶	Arrhythmias	Sensitization of the heart to catecholamines	A-59 A-76
Methoxyflurane (Penthrane)	Tetracycline	Nephrotoxicity	Unknown	A-138
Thiamylal (Surital)	Chlorpromazine	Orthostatic Hypotension	Additive	A-139
Anesthetics that depress neuromuscular transmission ²	Antibiotics that depress neuromuscular transmission ³	Respiratory arrest or prolonged neuromuscular blockade	Synergistic effects on neuromuscular transmission	A-61
Ether and curariform drugs ⁴	Antibiotics that depress neuromuscular transmission ³	Respiratory arrest or prolonged neuromuscular blockade	Synergistic effects on neuromuscular transmission	A-65 A-111
Succinylcholine	Echothiophate Iodide (Phospholine Iodide)	Prolonged apnea	Reduced pseudocholinesterase activity	H-229
Neuromuscular blocking agents	Quinidine or procainamide (given postoperatively)	Recurarization	Additive	A-152
<i>Analgesics (28:08)</i>				
Aspirin	Oral anticoagulants	Increased anticoagulant effect	Additive	A-155
Salicylates	Probenecid and Sulfapyrazone (Anturane)	Decreased uricosuric effect	Low doses of salicylates block inhibition of tubular reabsorption of uric acid	H-240 A-135
	Methotrexate	Increased serum level of free methotrexate	Displacement of methotrexate from binding sites	H-62
	Sulfonylurea antidiabetic agents	Enhanced hypoglycemic effect	Displacement of sulfonylurea from binding sites	A-26
Indomethacin	Aspirin	Decreased effect of indomethacin	Decreased and delayed absorption of indomethacin	A-87
	Probenecid	Increased serum level of indomethacin	Competition for same renal tubular excretory mechanism	A-88
Meperidine	Monoamine oxidase inhibitors ⁷	Excitation, convulsions, hypertension or hypo-	Unknown	A-101

CLINICALLY IMPORTANT DRUG INTERACTIONS

<i>Drug A</i>	<i>Drug B</i>	<i>Adverse Effect</i>	<i>Probable Mechanism</i>	<i>Reference</i>
Oxyphenbutazone (Oxalid, Tandearil)	Oral anticoagulants	tension, death (anecdotal reports only) Increased anticoagulant effect	Displacement of anticoagulants from binding sites	A-171
	Methandrostenolone (Dianabol)	Increased serum levels of oxyphenbutazone	Unknown	AS-387
Phenylbutazone (Azolid, Butazolidin)	Sulfonylurea antidiabetic agents	Enhanced hypoglycemic effect	Inhibition of microsomal enzyme activity	A-1
	Oral anticoagulants	Increased anticoagulant effect	Displacement of anticoagulants from binding sites	A-171
<i>Anticonvulsants (28:12)</i>				
Diphenylhydantoin (Dilantin) (DPH)	Chloramphenicol	DPH toxicity	Inhibition of microsomal enzyme activity	H-56
	Dicumarol	DPH toxicity	Competition for same metabolic degradation site	H-55
	Disulfiram (Antabuse)	DPH toxicity	Inhibition of microsomal enzyme activity	H-58
	Doxycycline (Vibramycin)	Decreased serum level of doxycycline	Induction of microsomal enzyme activity	Ref. 2
	Isoniazid	DPH toxicity	Inhibition of microsomal enzyme activity	A-51
	Thyroid hormone	Increased cardiac toxicity of thyroid	Displacement of thyroid from binding sites	H-179
Carbamazepine (Tegretol)	Doxycycline (Vibramycin)	Decreased serum level of doxycycline	Induction of microsomal enzyme activity	Ref. 2
<i>Antidepressants (28:16.04)</i>				
Tricyclic antidepressants ^a	Estrogens	Increased antidepressant effect	Unknown	Ref. 9
	Guanethidine (Ismelin)	Decreased hypotensive effect	Inhibition of uptake of guanethidine into adrenergic neurons	A-71
	Levodopa	Decreased antiparkinson effect	Impaired absorption and/or enhanced metabolism	In press
	Methylphenidate (Ritalin)	Increased serum levels of antidepressant	Inhibition of microsomal enzyme activity	H-200
	Monoamine oxidase inhibitors ⁷	CNS stimulation, hyperpyrexia, convulsions, coma, death (anecdotal reports only)	Unknown	A-7 AS-376
	Antipsychotic agents	Increased antipsychotic and/or antidepressant effect	Inhibition of microsomal enzyme activity	Ref. 10 Ref. 11
	Thyroid hormones	Increased antidepressant effect	Unknown	A-84
	Antidiabetic agents	Enhanced hypoglycemic effect	Unknown	AS-380
	Meperidine	Excitation, convulsions, hypertension or hypotension, death (anecdotal reports only)	Unknown	A-101
	Levodopa	Hypertensive crisis	Abrupt release of accumulated norepinephrine	A-95
Monoamine oxidase inhibitors ⁷	Sympathomimetic amines ⁶	Hypertensive crisis	Abrupt release of accumulated norepinephrine	H-185
	Tyramine in food	Hypertensive crisis	Abrupt release of accumulated norepinephrine	A-91
<i>Antipsychotic Agents (28:16.08)</i>				
Chlorpromazine	Guanethidine (Ismelin)	Decreased hypotensive effect	Displacement of guanethidine from site of action	Ref. 8
All agents	Thiamylal (Surital)	Orthostatic hypotension	Additive	A-139
	Tricyclic antidepressants ^a	Increased antipsychotic and/or antidepressant effect	Inhibition of microsomal enzyme activity	Ref. 10 Ref. 11
<i>Anorexiants and Analeptics (28:20)</i>				
Methylphenidate (Ritalin)	Tricyclic antidepressants ^a	Increased serum levels of antidepressant	Inhibition of microsomal enzyme activity	H-200

CLINICALLY IMPORTANT DRUG INTERACTIONS

<i>Drug A</i>	<i>Drug B</i>	<i>Adverse Effect</i>	<i>Probable Mechanism</i>	<i>Reference</i>
<i>Sedatives and Hypnotics (28:24)</i>				
Barbiturates	Adrenal corticosteroids	Decreased systemic effects of steroids	Inhibition of endogenous steroid production and induction of microsomal enzyme activity	A-83 A-34
	Oral anticoagulants	Decreased anticoagulant effect	Induction of microsomal enzyme activity	A-168
	Digitoxin	Decreased serum levels of digitoxin	Induction of microsomal enzyme activity	H-224
	Doxycycline (Vibramycin)	Decreased serum levels of doxycycline	Induction of microsomal enzyme activity	Ref. 1
	Griseofulvin	Decreased serum levels of griseofulvin	Unknown	A-68
Chloral Hydrate	Oral anticoagulants	Transient increase in anti-coagulant effect	Displacement of anticoagulant from binding sites	A-157 Ref. 6
Ethchlorvynol (Placidyl)	Oral anticoagulants	Decreased anticoagulant effect	Induction of microsomal enzyme activity	H-39
Glutethimide (Doriden)	Oral anticoagulants	Decreased anticoagulant effect	Induction of microsomal enzyme activity	A-162
<i>Diuretics (40:28)</i>				
Agents that cause potassium loss	Digitalis	Increased digitalis toxicity	Hypokalemia	A-38
Ethacrynic Acid (Edecrin)	Adrenal corticosteroids	Increased potassium loss	Additive	H-171
Furosemide (Lasix)	Aminoglycoside antibiotics ¹	Ototoxicity	Additive	A-93
Thiazide diuretics	Cephaloridine (Loridine)	Nephrotoxicity	Unknown	H-116
	Oral hypoglycemic agents	Reduced hypoglycemic effect	Unknown	A-29
<i>Agents Used in Gout (40:40)</i>				
Allopurinol (Zyloprim)	Mercaptopurine (Purinethol) and Azathioprine (Imuran)	Increased toxicity of anti-neoplastic drugs	Inhibition of xanthine oxidase	A-105
Probenecid	Aminosalicylic acid (PAS)	PAS toxicity due to increased blood levels	Inhibition of renal excretion	H-114
	Cephaloridine (Loridine)	Nephrotoxicity	Inhibition of renal excretion	H-115
	Indomethacin	Increased serum level of indomethacin	Competition for same renal tubular excretory mechanism	A-88
	Nitrofurantoin (Furadantin, Macrochantin)	Decreased efficacy of nitrofurantoin	Inhibition of renal tubular secretion of nitrofurantoin	A-114
	Salicylates	Decreased uricosuric effect	Low doses of salicylates block inhibition of tubular reabsorption of uric acid	H-240
Sulfinpyrazone (Anturane)	Salicylates	Decreased uricosuric effect	Low doses of salicylates block inhibition of tubular reabsorption of uric acid	A-135
<i>Antacids (56:04)</i>				
Antacids	Isoniazid	Decreased serum level of isoniazid	Delayed and depressed absorption	Ref. 3
	Tetracyclines	Decreased serum level of tetracyclines	Formation of non-absorbable complexes	A-136
Magnesium trisilicate	Ferrous sulfate	Reduced response to iron therapy	Impaired absorption of ferrous sulfate	H-232
Sodium bicarbonate	Tetracyclines	Decreased serum level of tetracyclines	Decreased dissolution and absorption of tetracycline	H-148
<i>Antidiarrheals (56:08)</i>				
Kaolin (Kaopectate)	Lincomycin (Lincocin)	Decreased serum level of lincomycin	Absorption of lincomycin	A-98
<i>Adrenal Corticosteroids (68:04)</i>				
All steroids	Barbiturates	Decreased systemic effects of steroids	Inhibition of endogenous steroid production and induction of microsomal enzyme activity	A-34 A-83
	Potassium-wasting diuretics	Increased potassium loss	Additive	H-171
<i>Androgens (68:08)</i>				
Anabolic steroids	Antidiabetic agents	Enhanced hypoglycemic effect	Unknown	H-71
C-17-alkylated androgens ¹²	Oral anticoagulants	Increased anticoagulant effect	Unknown	A-166

CLINICALLY IMPORTANT DRUG INTERACTIONS

<i>Drug A</i>	<i>Drug B</i>	<i>Adverse Effect</i>	<i>Probable Mechanism</i>	<i>Reference</i>
Methandrostenolone	Oxyphenbutazone (Oxalid, Tandearil)	Increased serum levels of oxyphenbutazone	Unknown	AS-387
<i>Estrogens (68:16)</i> All agents	Tricyclic antidepressants ⁸	Increased antidepressant effect	Unknown	Ref. 9
<i>Antidiabetic Agents (68:20)</i> All agents	Anabolic steroids	Enhanced hypoglycemic effect	Unknown	H-71
	Monoamine oxidase inhibitors ⁷	Enhanced hypoglycemic effect	Unknown	AS-380
	Propranolol (Inderal)	Enhanced hypoglycemic effect	Impairment of counter-regulation	AS-378
	Alcohol	Enhanced hypoglycemic effect	Unknown	A-121 A-144
Oral agents	Thiazide diuretics	Reduced hypoglycemic effect	Unknown	A-29
Sulfonylurea antidiabetic agents ⁵	Chloramphenicol	Enhanced hypoglycemic effect	Inhibition of microsomal enzyme activity	A-28 AS-399
	Dicumarol	Enhanced hypoglycemic effect	Inhibition of microsomal enzyme activity	H-73
	Phenylbutazone (Azolid, Butazolidin)	Enhanced hypoglycemic effect	Inhibition of microsomal enzyme activity	A-1
	Salicylates	Enhanced hypoglycemic effect	Displacement of sulfonylurea from binding sites	A-26
	Sulfaphenazole (Sulfabid) and sulfisoxazole (Gantrisin)	Enhanced hypoglycemic effect	Displacement of sulfonylurea from binding sites	A-147
<i>Thyroid Hormones (68:36)</i> All agents	Cholestyramine (Cuemid, Questran)	Reduced response to thyroid therapy	Binding in gastrointestinal tract	A-143
	Diphenylhydantoin (Dilantin)	Increased cardiac toxicity of thyroid	Displacement of thyroid from binding sites	H-179
	Oral anticoagulants	Increased anticoagulant effect	Unknown	A-174
	Tricyclic antidepressants ⁸	Increased antidepressant effect	Unknown	A-84
<i>Vitamins (88:00)</i> Pyridoxine	Levodopa	Decreased antiparkinson effect	Increased decarboxylation of levodopa peripherally	A-96
<i>Miscellaneous</i> Alcohol	Antidiabetic agents	Enhanced hypoglycemic effect	Unknown	A-144
Disulfiram (Antabuse)	Oral anticoagulants	Increased anticoagulant effect	Inhibition of microsomal enzyme activity	H-24
	Diphenylhydantoin (Dilantin) (DPH)	DPH toxicity	Inhibition of microsomal enzyme activity	H-58
Echothiophate Iodide (Phospholine Iodide)	Succinylcholine	Prolonged apnea	Reduced activity of pseudocholinesterase	H-229
Tyramine in foods	Monoamine oxidase inhibitors ⁷	Hypertensive crisis	Abrupt release of accumulated norepinephrine	A-91

1. Aminoglycoside antibiotics include gentamicin, kanamycin, neomycin, and streptomycin.
2. Antibiotics that depress neuromuscular transmission include colistimethate, kanamycin, paromomycin, polymixin B, streptomycin, and viomycin.
3. Anesthetics that depress neuromuscular transmission include cyclopropane, fluroxene, halothane, and methoxyflurane.
4. Curariform drugs include gallamine, succinylcholine, and tubocurarine.
5. Sulfonylurea antidiabetic agents include acetohexamide, tolazamide, chlorpropamide, and tolbutamide.
6. Sympathomimetic amines include amphetamines, ephedrine, epinephrine, isoproterenol, methylphenidate, norepinephrine, phenylephrine, and tyramine in foods; sympathomimetic amines are also found in many nonprescription cough, cold, and sinus remedies, including nasal decongestants.
7. Monoamine oxidase inhibitors include isocarboxazid, pargyline, phenelzine, and tranylcypromine.
8. Tricyclic antidepressants include amitriptyline, desipramine, doxepin, imipramine, nortriptyline, and protriptyline.
9. Drugs related to amphetamine include ephedrine, methylphenidate, and methamphetamine.
10. Adrenergic drugs that act mainly by releasing norepinephrine include ephedrine, mephenteramine, metaraminol, and methamphetamine.
11. Halogenated hydrocarbon anesthetics include chloroform, ethyl chloride, fluroxene, halothane, methoxyflurane, and trichloroethylene.
12. C-17-alkylated androgens include methandrostenolone, norethandrolone, and oxymetholone.

ACKNOWLEDGMENT

I am indebted to Dr. David J. Greenblatt of the Clinical Pharmacology Unit, Massachusetts General Hospital, for making many useful suggestions and critically reviewing the manuscript.

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THE HAIRLESS, ODORLESS AXILLA: AN EXAMPLE OF SELECTIVE END-ORGAN UNRESPONSIVENESS TO ANDROGEN — *Continued from Page 11*

thought to be controlled by adrenal androgens.² Affected females in the present kindred all have normal pubic hair and would thus not be expected to have decreased androgens. Normal 17-ketosteroids have, in fact, been demonstrated in the three cases who could be studied. One possible explanation for the failure of hair and sweat to appear in the axillae might be a relative end-organ unresponsiveness under the control of a specific gene. Since males apparently are not affected even when known to have the gene, then possibly exogenous androgen would stimulate axillary activity in affected females. If a male were homozygous for this characteristic, then he might also show the phenotype.

For the moment, this genetic aberration repre-

sents an interesting and harmless variation from the normal. One might go one step further in view of the amount of money and energy spent in deodorizing and depilating normal axillae and say that this phenotype is desirable. Possibly at some point in the future when genes may be selectively plucked from their chromosomes, this characteristic may become the rule rather than the exception.

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Health educators and providers alike have generally come to the conclusion that for a preventive system of health care to work effectively, the health consumer himself must first be aware of, and be responsible for, primary preventive maintenance of his own health.

A new public television program which has received strong support from many health agencies, including Maine Blue Cross and Blue Shield, is currently being aired on both WCBB and the Maine Public Broadcasting Network, and is designed to show viewers in a very entertaining way how to care for their own health.

The experimental series — 26 hour-long shows to be broadcast each week for a full year — has been characterized as television’s most ambitious attempt to both inform people and motivate them toward healthier living.

It is the first program to be created for adults by CTW, pioneers of such successful TV productions as “Sesame Street” and “The Electric Company.”

Feeling Good will employ a variety-magazine format using animation, song, dance, comedy and documentaries to treat 11 priority health topics: alcohol abuse, cancer, child care, exercise, dental care, the health care delivery system, heart disease, hypertension, mental health, nutrition and prenatal care. Each topic will be treated several times during the series’ first year.

Several informational and behavioral goals have been developed for each topic. The aim is to inform people about the symptoms and methods of avoiding various health problems to motivate them to take some actions in preventing their occurrence or to decrease their danger.

The underlying philosophy of Feeling Good is that people have more control over their health than they realize. The show will point out some of the fundamentals of good health and then will pinpoint how people’s actions play an important role in the kind of health they enjoy.

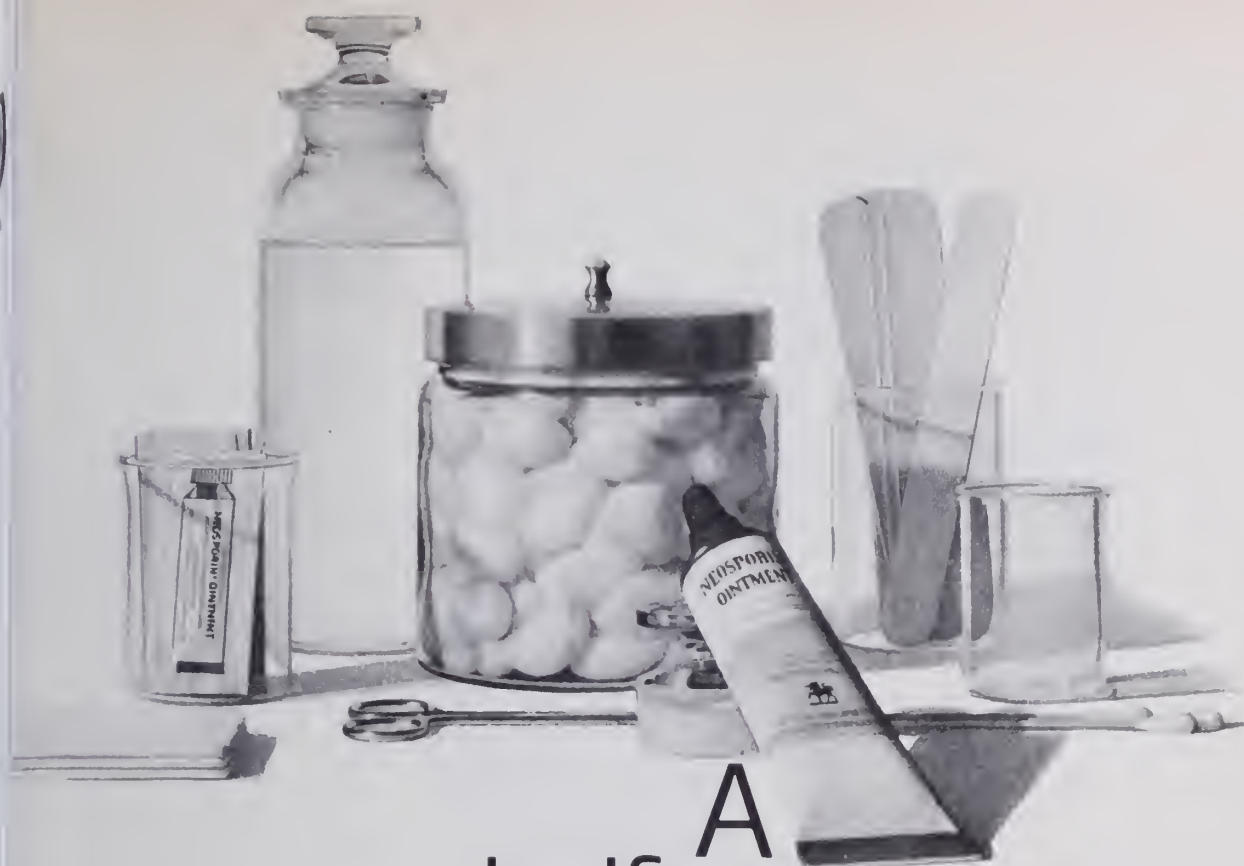
Primary target audience for the series is young parents who play major roles in influencing the health of their immediate families. Of particular concern to the producers are the health problems of low-income families.

Major underwriters are the Corporation for Public Broadcasting, the Robert Wood Johnson Foundation, Exxon Corporation, and the Aetna Life and Casualty Company. Local WCBB broadcast costs are covered through a grant from Maine Blue Cross and Blue Shield.

CTW plans an extensive national outreach project centered on local public television stations. This will involve cooperation with national health organizations and unions and with community level medical, health and education groups.

The Workshop’s community education service division (CES) which operates seven regional offices across the country staffed by specialists in outreach work with the urban and rural poor, will help draw attention to the programs and encourage community members to take advantage of the information and assistance they provide.

Seminars, briefings, and distribution of promotional and health information literature are among activities planned for the health series. We urge you to extend the potential effectiveness of the series by making your patients aware of it. Further information about the series can be obtained from your nearest Public Television station or Maine Blue Cross and Blue Shield.



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INDICATIONS: Therapeutically, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms in: • infected burns, skin grafts, surgical incisions, otitis externa, pyoderma (impetigo, ecthyma, sycosis vulgaris, paronychia) • Secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • Inflammatory lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically*, the ointment may be used to prevent bacterial contamination of wounds, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and lacerations accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity of neomycin, care should be exercised when using this product in treating severe burns, trophic ulceration and other extensive conditions where

absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



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The Role of the Detail Man

"I may be prejudiced, but I am very much in favor of the detail men I meet. Most of them are knowledgeable about the drugs they promote and can be a great help in acquainting me with new medication."

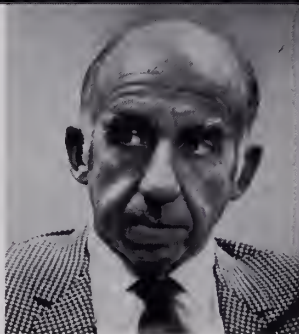
Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.

Dr. Willard Gobbell
Family Physician
Encino, California



Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School



"In the total picture of dealing with health problems in this country there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce — information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love — they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.*, the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

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County Society Notes

ANDROSCOGGIN

The September meeting of the Androscoggin County Medical Association was held at Steckino's Restaurant, Thursday, September 19, 1974. The meeting was called to order by the President, Dr. Gerard L. Morin, at 7:55 p.m., with 34 members present.

The minutes of the previous meeting were read and accepted.

Letters from Dr. Reeves regarding communicable diseases were read. A letter from Dr. Charles A. Hannigan regarding legal representation for Medicare was read.

Members volunteering for serving on Legislative Committee: Drs. Margaret H. Hannigan and Ross W. Green.

Dr. Hannigan suggested Scabies and Dr. Carrier suggested Carcinoma as discussion problems for WCBB.

Report of the Annual House of Delegates Meeting was given by Dr. Thomas F. Shields. The membership was informed of Dr. Charles Steele's honor in receipt of the Annual Blue Cross-Blue Shield Award.

Dr. Herbert J. Wright, Jr. was appointed to the chairmanship of PTO.

The 1974 Resolution regarding Mental Health Care was referred to the Fall Meeting of the M.M.A. House of Delegates.

The 1974 Resolution requesting that 3rd Party Insurance companies be reimbursed equally for services in hospital and office was approved by the House of Delegates. Dr. Andre P. Marcotte suggested that if an important proposal is to be made to the House of Delegates, that we must provide sufficient representation to push for passage. General discussion ensued. Suggestion has been made that close watch be kept for important resolutions or legislation and people be picked to represent us.

A motion was made and seconded that Diabetes Week be observed. Dr. Ralph Zanca was nominated and duly voted as Chairman for Diabetes Week in Androscoggin County.

Drs. Richard J. Muttly and Cheong K. Leong were voted to membership in Androscoggin County and Maine Medical Association.

Discussion relative to indiscreet interviews was discussed. Dr. Daniel R. Shields moved to create a committee of 3 men, including 1 member from the credential committee of each hospital to discuss ethical conduct for announcing office opening or publicity. The Amendment Committee should make guidelines in printed form to be given to each applicant and both hospitals. This was seconded and voted. Original motion seconded and voted.

New Business: Dr. Charles Hannigan — Discussion about Maine Medical School Fund decision that Maine go it alone and carry the first 2 years. May expect student in Fall, 1976.

Dr. Margaret Hannigan suggested that we have greater representation on the Maine Medical School Committee.

Dr. Stanley D. Rosenblatt raised the question of a new contract being written by Blue Shield as to 80 percent of usual and reasonable fees with certain individuals getting service benefits.

It has been suggested that the October meeting be Husband and Wife dutch treat dinner with program by members involved in Family Practice Residency.

Nominating Committee appointed: Drs. John W. Carrier, Chairman; Gilbert R. Grimes and Thomas F. Shields.

Meeting was adjourned at 9:25 p.m.

LOUIS N. FISHMAN, M.D., *Secretary protem*

The October meeting of the Androscoggin County Medical Association was held at Steckino's Restaurant, Thursday, October 17, 1974. The meeting was called to order by the President, Dr. Gerard L. Morin, at 8:00 p.m., with 32 members and their ladies present. Guests for the evening were Dr. John D. Denison, Dr. and Mrs. C. Philip Lape, and Dr. and Mrs. Eric Goranson of the Family Practice Residency Program.

A very short business meeting was held following a fine supper. All present then enjoyed a very informative discussion of the Family Practice Residency Program presented by Drs. Lape and Denison. Dr. Eric Goranson discussed his views of the program from the Resident's position.

A lively forum which included the ladies present followed.

The meeting was adjourned at 9:45 p.m.

RICHARD M. SWENGEL, M.D., *Secretary*

CUMBERLAND

The 388th meeting of the Cumberland County Medical Society was held on September 19, 1974 at the Homewood Inn in Yarmouth, Maine. There were approximately 110 members and guests in attendance at our annual outing.

A hotly contested softball game ended with a final score of 24 to 5. Some of the outstanding Little Leaguers involved in the contest were John Bischoffberger, Paul Marston, Tom Martin, Sr. and our perennial umpire Van. Following the game, the dinner was served and multiple helpings of lobster and steak consumed by our starving membership.

Under the able direction of Stuart McGuire, Master of Ceremonies and lead singer, the Clam Flats presented an hour of lively entertainment. John Godsoe shone at the trumpet while Wes English banged on the banjo. Joe Stocks tinkled the ivories and Phil Whitney played a soulful saxophone. Last but not least was Dave Hotelling in the percussion section.

Many of Stu's stories would bear repeating but not in this column.

ALFRED E. SWETT, M.D., *Secretary*

YORK

The October meeting of the York County Medical Society was held at the York Hospital, York, Maine on Wednesday, October 9, 1974. The format was as follows: Social Hour 6:30 p.m., Dinner 7:30 p.m., Business Meeting followed presided over by Dr. Carl E. Richards of Sanford, President of the York County Medical Society.

The speakers were: Terry Gendron, R.N. of Sanford who spoke on "Down's Syndrome," and Frank Long, Senior Medicare Representative, Union Mutual Medicare Department, Portland, Maine who spoke on "Medicare — How It Relates to the Physician." He was assisted by Richard Hilton, an associate.

There was extensive audience participation replete with questions and answers following these speakers.

Dr. James H. Stuart of York, Maine was accepted into membership.

There were 18 physicians and 6 guests present. Two new physicians from York, Maine were introduced. They are Drs. Dennis Adamis and Thomas Chayka.

It was announced that the combined Annual Meeting of the York County Medical Society and its Auxiliary will be held on January 8, 1975 at the Cascade Inn, Saco, Maine with a Social Hour at 6:30 p.m., Dinner at 7:30 p.m. and separate business meetings to follow. There will be a prominent speaker and dancing to follow.

It was also announced that Diabetes Week was to be observed November 17th to 23rd. All physicians were urged to participate in this program.

The Committee in charge of arrangements for this meeting was made up of Drs. Kenneth E. Leigh and Lawrence R. Hazzard, both of York, Maine.

The meeting, a most interesting one, was adjourned at 10:10 p.m.

MELVIN BACON, M.D., *Secretary*



The Journal of the Maine Medical Association

Volume Sixty-six

Brunswick, Maine, February 1975

Number 2

The Use of Equalization Tubes in Nonsuppurative Otitis Media

LORING W. PRATT, M.D., F.A.C.S.*

Nonsuppurative otitis media, alias serous otitis media, secretory otitis media and catarrhal otitis media, is one of the most common affections of the middle ear. It is a common effusion of sterile fluid within the middle ear of the greatest economic significance because it affects small children in great numbers.

Because its primary symptom is hearing impairment, the impact of this disease is chiefly upon a group of individuals at a crucial time in their lives so far as learning and development is concerned. Impairment of hearing at this age may subtly, but surely, transform a bright into a slow, and a slow into a retarded child. The retarded may become classified as untrainable rather than trainable or educable. Thus, hearing impairment, from whatever cause, degrades the ability of the individual to learn.

The hearing impairment of nonsuppurative otitis media is correctable and it is therefore crucial that this problem be recognized promptly and accurately treated to minimize the resulting economic and personal loss.

Early efforts to prevent healing of the myringotomy incision were made by Saissy who introduced a catgut string into the middle ear via the myringotomy to keep the wound from healing. Fishbone plugs and lead wires were also used.¹

Politzer introduced a hard rubber eyelet in the 1860's. This was a hollow, grooved rubber stent designed to keep the myringotomy wound from healing. These procedures were not highly successful and it was not until the 1950's when inert plastic materials made the use of equalization

tubes practical.^{2,3} Common use of the operating microscope and appropriate instrumentation, implementing the concept of circumventing the obstructed eustachian tube, all forwarded the use of equalization tubes, and made it the common procedure it is today.

The etiology of all forms of nonsuppurative otitis media is eustachian tube incompetence, which may occur for many different reasons. It commonly results from:

1. Upper respiratory infection
 - A. Purulent
 - B. Viral
2. Allergic rhinitis
 - A. Hyperplastic rhinitis
 - B. Allergic polypsis
3. Sinusitis
 - A. Acute
 - B. Chronic
4. Adenoid
 - A. Chronic infection
 - B. Hypertrophy
5. Tumors of nasopharynx
 - A. Benign
 - B. Malignant
 1. Cancer

The incidence of infectious problems producing nonsuppurative otitis media is much greater in children, because the child's eustachian tube is anatomically shorter, relatively more open, and located more horizontally than that of an adult (Figs. 1,2). This permits infection to ascend more readily from the infant nasopharynx to infect and obstruct the eustachian tube, giving rise to nonsuppurative as well as to suppurative disease of the middle ear.

The anatomical structure of the eustachian tube bears on this problem.⁴ The orifice of the cartilagi-

*Chairman, Department of Otolaryngology, Thayer Hospital, Waterville, Maine 04901.

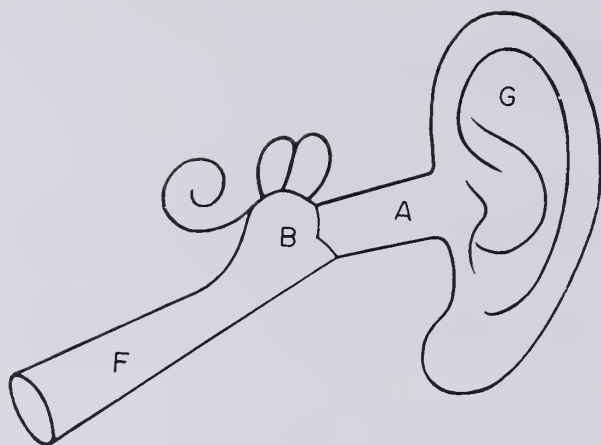


Fig. 1. Diagram showing short, nearly horizontal, relatively wide eustachian tube typical of infant.

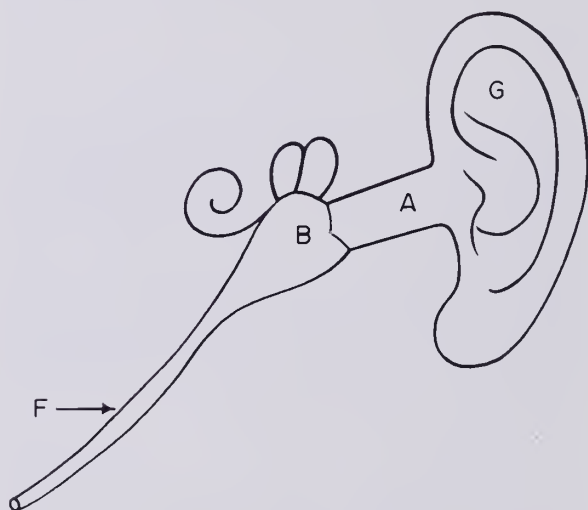


Fig. 2. Diagram showing large, more nearly vertical, relatively narrow eustachian tube typical of adult.

nous part of the tube, the torus tubarius, protrudes into the nasopharynx where its posterior wall, the ala tuba, moves into the Fossa of Rosenmuller on swallowing. The presence of a mass of adenoid tissue in the Fossa of Rosenmuller interferes with its proper opening to allow air to pass up into the middle ear. This explains why a large midline mass of adenoid, which does not fill the Fossa of Rosenmuller, does not necessarily interfere with the function of the eustachian tube.

In its medial portion the eustachian tube passes through a cranial foramen and, being completely surrounded by bone, frequently becomes occluded by inflammatory changes which take place within its mucosal or submucosal structure.⁵ The presence of deposits of lymphoid tissue within the submucosal stoma of the eustachian tube provides an added source of swelling and obstruction to the passage of

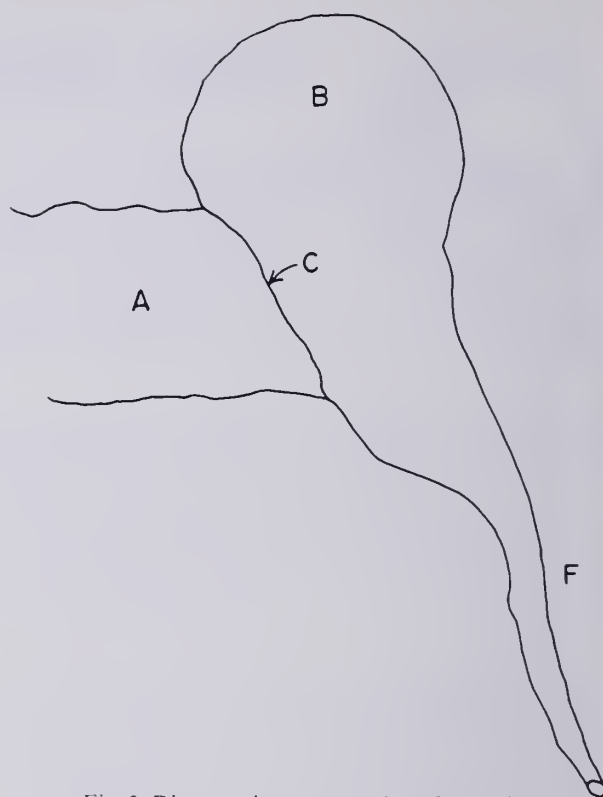


Fig. 3. Diagrammatic representation of normal ear
A. External auditory canal
B. Middle Ear
C. Tympanic membrane
F. Eustachian Tube — unobstructed

air up the lumen of the eustachian tube into the middle ear.

Normal physiological function requires an air filled middle ear with internal pressure essentially equal to that of the ambient pressure in the external ear canal. When pressure within the middle ear is reduced, the tympanic membrane is pulled in or retracted and does not vibrate as efficiently as when internal and external pressure are equal, leaving the tympanic membrane suspended with maximum amplitude of vibration possible (Figs. 3 and 4). If pressure is increased within the middle ear (a rarely encountered clinical situation except in acute otitis media, purulent) the same restriction of tympanic membrane motion ensues.

Alteration of middle ear pressure, without equalizing it with ambient external air pressure, interferes with the transmission of sound vibrations and impairs the hearing.

If reduced pressure within the middle ear persists for a prolonged period, not only is the tympanic membrane retracted, but serous fluid accumulates in the middle ear as a result of transudation of fluid from the capillary bed. The transudate lies free in the middle ear cavity (Figs. 5 and 6).

In more prolonged cases, the transudate becomes inspissated and the epithelium of the middle ear

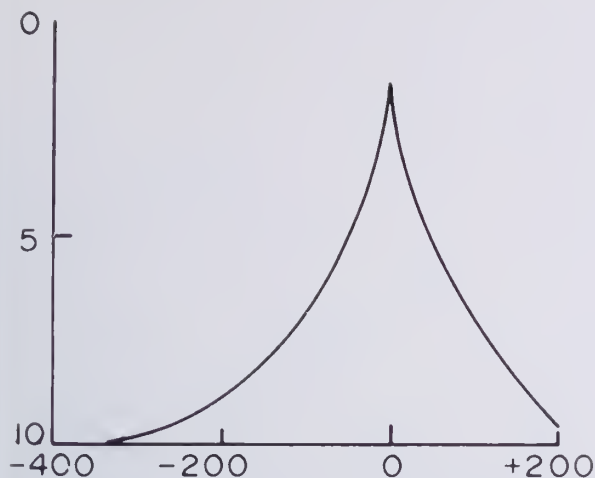


Fig. 4. Tympanographic curve showing normal middle ear function with peak at approximately 0 mm of H_2O pressure. Type A Curve.

mucosa undergoes metaplasia producing excessive numbers of goblet cells.^{7,8} These glands produce thick mucus and the fluid within the middle ear becomes thick and sticky and is known as "glue ear." If the long standing effusion has become contaminated by blood, the blood pigment contributes to a Prussian blue appearance of the tympanic membrane and contained middle ear fluids. This is known as "blue ear drum."⁹

Acute eustachian tube obstruction resulting from, or associated with, barotrauma sometimes causes capillary rupture and fresh blood is seen in the middle ear, as well as small hemorrhagic areas within the tympanic membrane.

There are two types of nonsuppurative otitis media, acute and chronic. Acute nonsuppurative otitis media may be due to sudden acute eustachian tube obstruction secondary to acute bacterial or viral upper respiratory obstruction. This sudden obstruction also occurs at times in association with episodes of acute allergic disease.

In the presence of barotrauma, an eustachian tube which had previously been functioning in adequate fashion, may suddenly become incompetent and acute nonsuppurative otitis media ensues. This occurs in both flying and diving.

The usual sequence of events is that, on ascent, air streams freely from the eustachian tube into the nasopharynx, but on descent, air is not transported to the middle ear via the eustachian tube. If the individual is unable to forcefully clear his ears by yawning, tongue and jaw movements, or by Valsalva maneuver, the eustachian tube obstruction may persist and acute nonsuppurative otitis media results. With the establishment of reduced pressure in the middle ear, the series of events outlined above occurs and nonsuppurative otitis media is the inevitable result. There is a great deal of hazard to those who fly or dive in the presence of acute upper

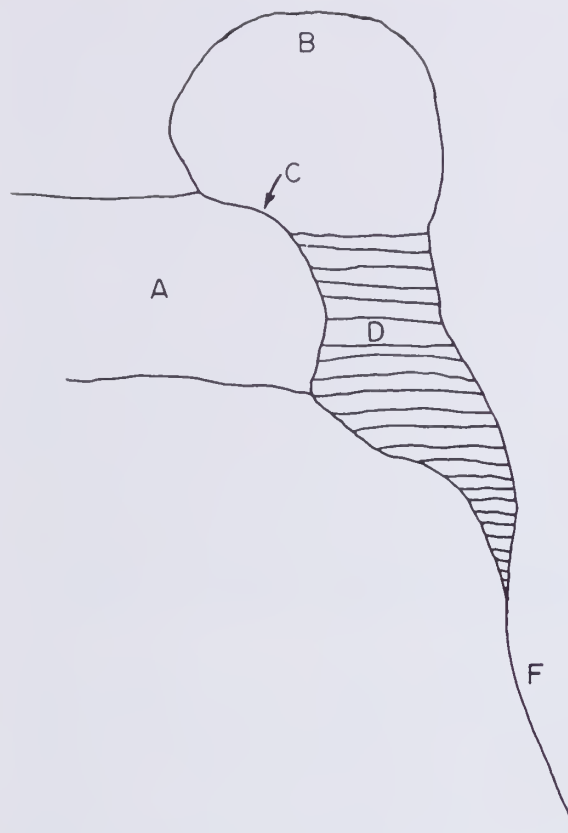


Fig. 5. Diagrammatic representation of middle ear in case of non-suppurative otitis media

- A. External auditory canal
- B. Middle ear
- C. Retracted tympanic membrane
- D. Fluid transudate in middle ear
- F. Obstructed eustachian tube

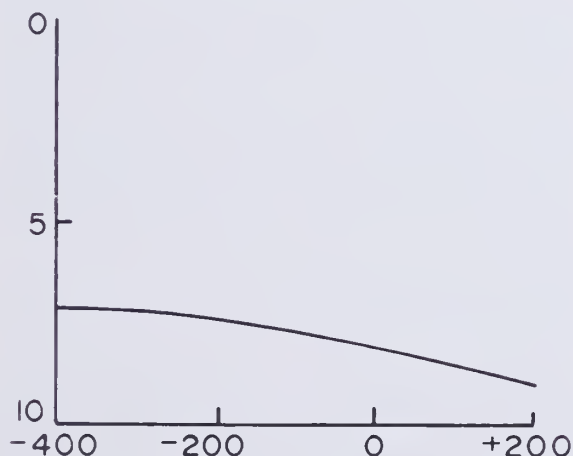


Fig. 6. Tympanographic curve showing flat curve demonstrating almost complete lack of motion of the tympanic membrane. Type B Curve.

respiratory infection, sinusitis or allergic flareups.

Although pressure changes involved in both diving and flying are significant, the maximum pressure change in flying must be of a magnitude equal to or less than one atmosphere. Most flying produces

changes far less than one atmosphere. In diving, however, the maximum usual pressure change is under ten atmospheres, but under extreme diving conditions may possibly change as much as twenty atmospheres. Fluctuations of one to four atmospheres of pressure change are common.

The problems encountered in flying and diving are the same. Sudden acute reduced pressure within the middle ear produces a transudate or exudate of fluid and often capillary rupture and bleeding into the middle ear and within the substance of the tympanic membrane. These changes affect the mastoid air cells and their mucosal lining with equal severity.

Chronic nonsuppurative otitis media occurs most commonly in children, but may be seen in adults as well. The disease is the same and is managed in the same way.

Eustachian tube obstruction prevents adequate ventilation of the middle ear. Blood circulation through the mucosa of the middle ear dissolves oxygen from the middle ear cavity thus reducing the pressure within the cavity, and both transudate and exudate result.

In long standing chronic eustachian tube obstruction, there often is thick mucoid material which fills the middle ear and impairs the sound transmission mechanism by means of the presence of a mass of thick viscid material. This material impairs the transmission of vibrations of both the tympanic membrane and the auditory ossicular chain, in addition to retracting the tympanic membrane. This is the entity commonly called "glue ear."

The diagnosis of nonsuppurative otitis media is made on the basis of several findings.

In acute disease, the history is usually that of a stuffy ear following a cold or allergic flareup. The history associated with flying is that of difficulty "clearing" the ears on descent. Among divers, the problem of clearing the ear on descent is often then complicated by further difficulty "clearing" on the ascent. There is usually the association of pain, sometimes severe, in the ear and mastoid region, when the problem arises in association with flying or diving.

In the less acute form produced by respiratory infection or allergic disease, there is usually no associated pain.

In both cases, the patient complains of autophony, hearing impairment, and a stuffy sensation which involves the whole side of the head. Sometimes the sensation of fluid moving within the middle ear is noted.

In chronic nonsuppurative otitis media, the complaint is usually only that of hearing loss. Sometimes there is complaint of a stuffy sensation in the head, but more often there is no complaint from the patient, who is more than likely a child. It is usually the school teacher or the parent who requests consultation because of hearing impairment.

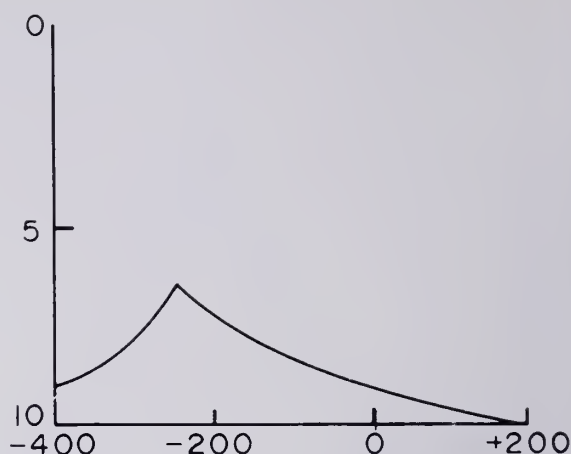


Fig. 7. Tympanographic curve showing normal middle ear function, but peaking at -200mm of H₂O pressure. Type C Curve.

SYMPTOMS

1. Acute nonsuppurative otitis media
 - A. Hearing impairment
 - B. Stuffy ear
 - C. Autophony
 - D. Discomfort, and/or stuffiness in side of head
 - E. Pain
2. Chronic nonsuppurative otitis media
 - A. Hearing impairment
 - B. Stuffy ear
 - C. Autophony

Although the diagnosis of nonsuppurative otitis media is suggested by the history, the definitive diagnosis is made by further study of the ear. Examination of the ear by otoscopy reveals an essentially normal or slightly injected tympanic membrane which is retracted. Behind the drum head may be seen amber or yellowish fluid, sometimes with bubbles in the middle ear or occasionally, in the acute form, fresh blood or old blood may be seen. Severe chronic disease occasionally causes blood pigment to be liberated into the middle ear, producing the characteristic "blue ear" drum head.

Pneumatic otoscopy is a useful, simple procedure which readily reveals limitation of motion of the tympanic membrane.

Tuning fork tests may give a variety of results, depending upon the severity of the disease. These tests should be made with a 512 DV(C-2), preferably steel, tuning fork. Air conducted sound may be better than bone conducted sound in mild problems, but bone conducted sound is heard better than air conducted sound in the more prolonged or severe problems. The Weber test lateralizes to the most severely involved ear, but remains midline in disease which is equally severe in each ear.

Pure tone audiometry is nearly normal in mild cases and may show that air conduction is better than bone conduction. This is especially true if there

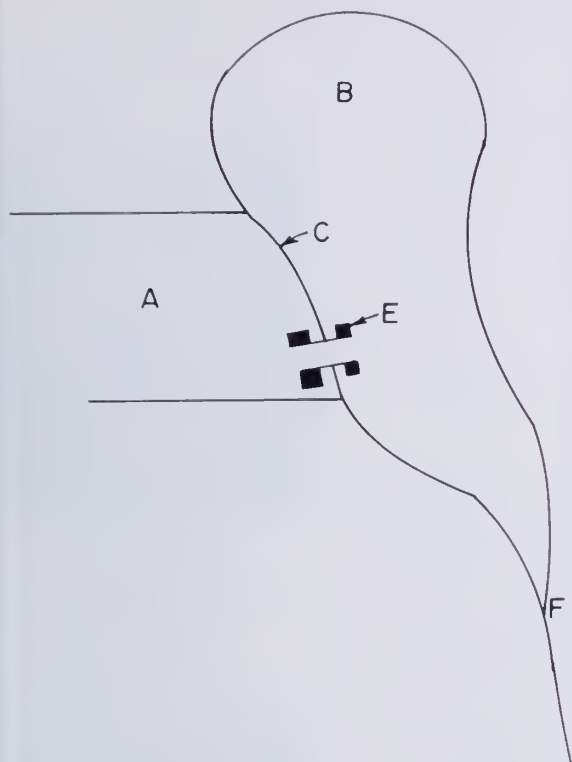


Fig. 8. Diagrammatic representation of middle ear showing equalization tube in place

- A. External auditory canal
- B. Middle ear
- C. Tympanic membrane in normal position
- E. Equalization tube
- F. Obstructed eustachian tube

are air bubbles in the middle ear. Severe disease markedly impairs the sensitivity of air and bone conduction at normal levels.

Impedance audiometry, which normally produces a Type A Curve (Fig. 4), shows either a Type B or a Type C Curve (See Figs. 6 and 7). The Type C Curve is found in those ears which contain bubbles of air, and the reading is considered significant if the curve peaks at a negative pressure of minus 150mm of H₂O or more. The Type B Curve is seen in ears which are completely full of fluid, in which the tympanic membrane is virtually immobile.

The treatment of nonsuppurative otitis media has two objectives. The first is the relief of the pressure differential between the external ear canal and the middle ear. This may be accomplished by the use of nasal vasoconstrictors, systemic vasoconstrictors, antihistamines and Valsalva maneuver. Catheterization of the eustachian tube with inflation and/or bougienage has been used in the past, but is not in favor today.

Current definitive therapy consists of paracentesis of the tympanic membrane, aspiration of fluid contained within the middle ear and the insertion of a plastic tube through the opening made in the tympanic membrane, so that as the incision heals, the

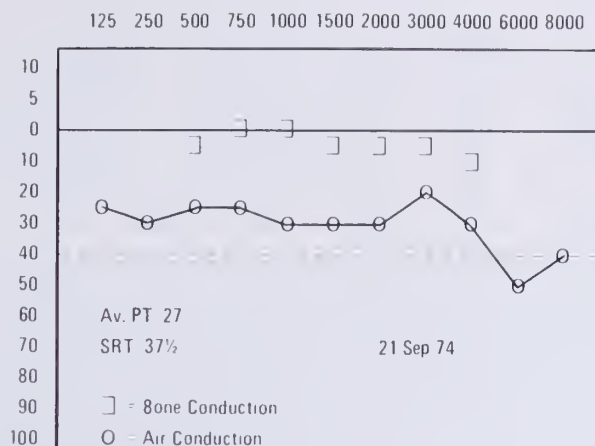


Fig. 9. Diagram showing conductive hearing loss secondary to nonsuppurative otitis media.

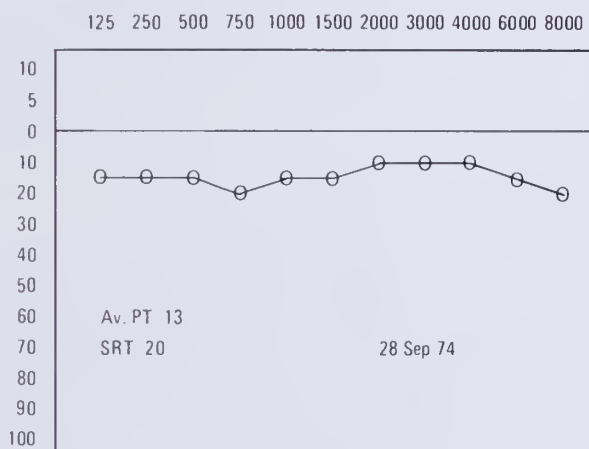
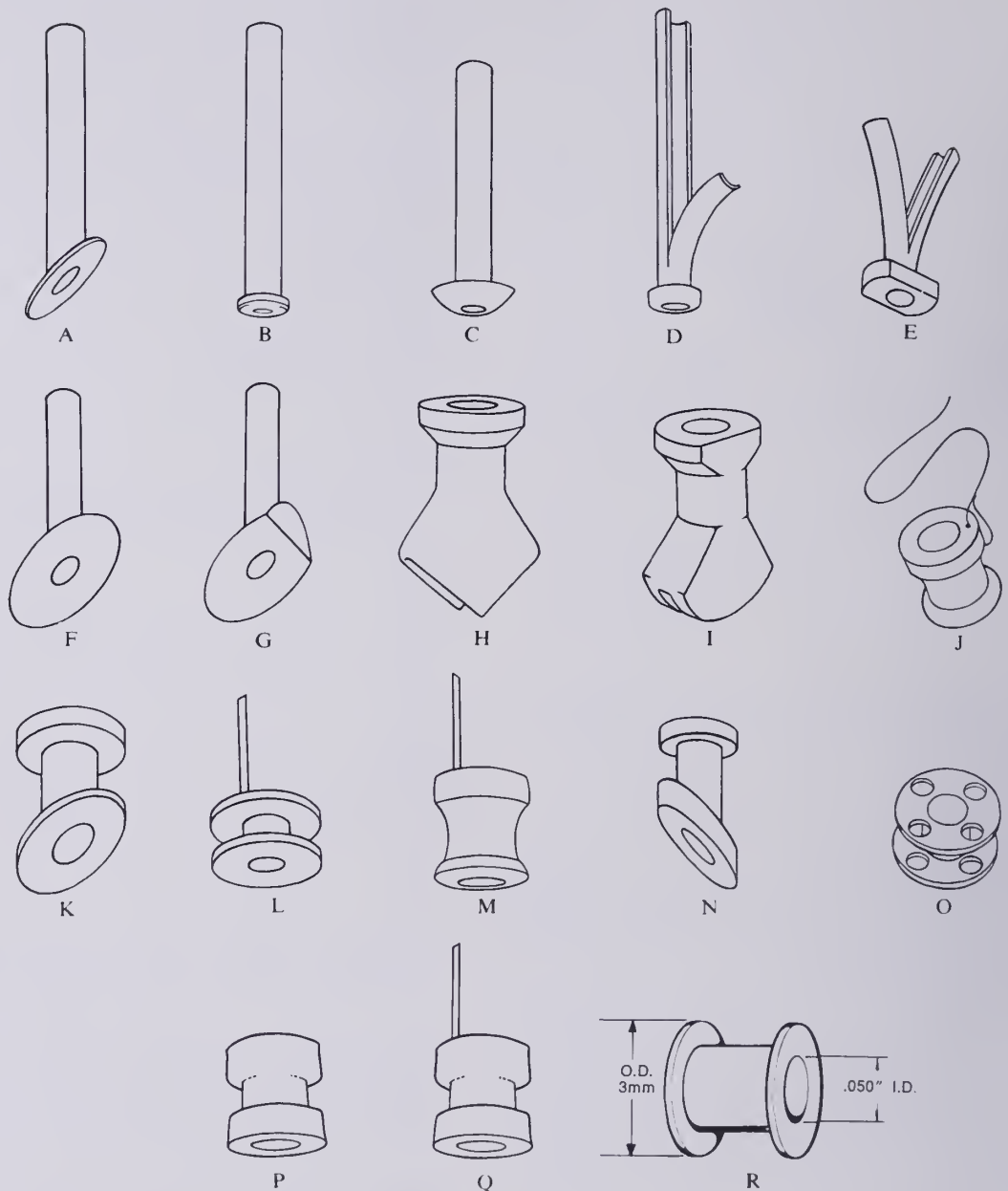


Fig. 10. Diagram showing audiogram of same patient as in Figure 6, three days after insertion of equalization tube into middle ear.

membrane heals around a plastic tube that provides a channel through which air may pass from the external canal into the middle ear, and thus equalize the pressure between the middle ear and the external canal. This promptly improves the hearing^{11,12} (Figs. 8, 9 and 10). This procedure is customarily performed with the aid of the operating microscope, and the incision and the equalization tube are located in the anterior inferior quadrant of the tympanic membrane. There is a great variety of tubes (Fig. 11) which are used, but the purpose and underlying principle of each is the same. The exact shape of the tube is not important, but it would seem the essential characteristics of a tube would be an adequate lumen to permit equalization of air pressure within the middle ear, a flange large enough to retain the tube, a minimal mass of foreign body in the middle ear, an inert material which produces no inflammatory change and which does not collect secretions which may obstruct its lumen. The tubes are either extruded spontaneously or are removed

Fig. 11. Illustrations showing variety of tubes available for use as ventilating tubes.



- A. Armstrong — beveled grommet — long.
- B. Regular — small ventilating tube.
- C. Regular — large ventilating tube.
- D. Fuerstein ventilating tube.
- E. J. S. K. split teflon drain tube.
- F. Perlee — long term — posterior placement.
- G. Perlee — long term — anterior superior placement.
- H. Arrow — Lindeman — Silverstein.
- I. Gross.
- J. Shepard drain tube with steel wire.
- K. Armstrong beveled grommet — short.
- L. Collar button with molded plastic bristle for aid in removal.
- M. Shepard grommet with molded plastic bristle for aid in removal.
- N. Armstrong — beveled grommet.
- O. Reuter bobbin — stainless steel for long term use.

- P. Donaldson tube.
- Q. Donaldson tube with molded plastic bristle for aid in removal.
- R. Collar button tube — to illustrate actual sizes of tubes.

All of these tubes are used with the lower end (as drawn) through the tympanic membrane. In all cases, this is the small flange, with the exception of H and I, where the large mass of the tube is placed within the middle ear. These tubes (H and I) are so used to prevent an atelectatic middle ear from applying the flange of the tube to the promontory and thus obstructing its lumen.

These diagrams were redrawn from illustrations used in the catalogues of Richards Manufacturing Company, Memphis, Tennessee and Xomed Division of Xomox Corporation, Cincinnati, Ohio. The illustrations are used with their permission.

Continued on Page 35

WHEN FLU HITS AND HURTS

HERE

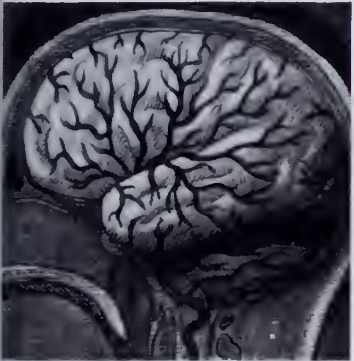
Muscles
and joints




Wherever it hurts, Empirin Compound with Codeine usually provides the symptomatic relief needed.

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In flu and associated respiratory infection, Empirin Compound with Codeine provides an intuitive bonus in addition to relief of pain and bodily discomfort.

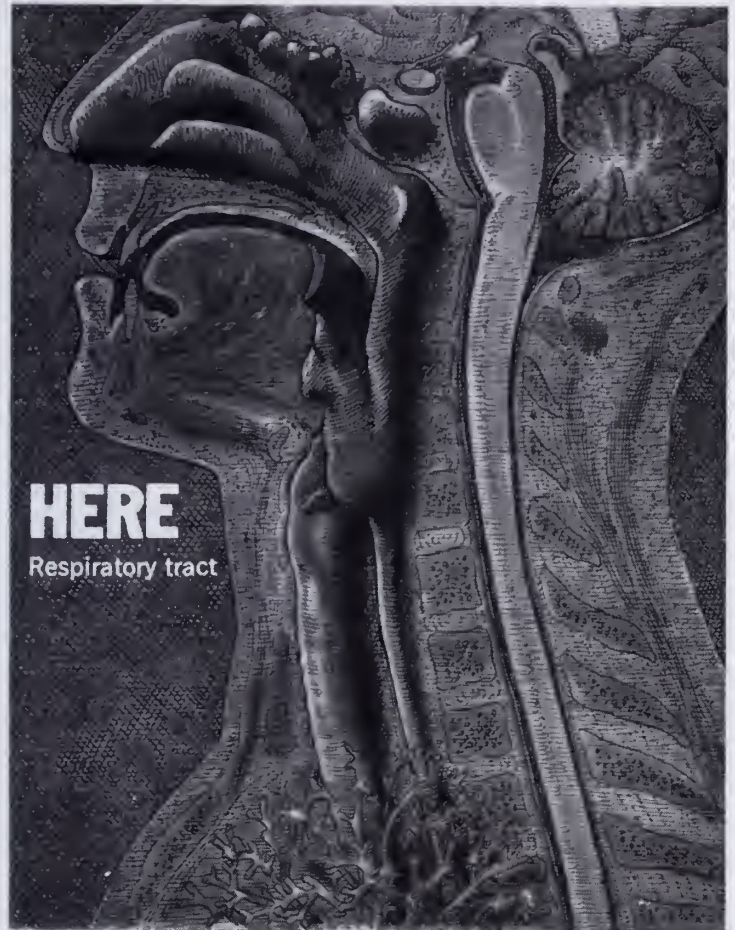
 **prescribing convenience:** up to 5 refills in 6 months, at your discretion (unless restricted by state law); by telephone order in many states.

Empirin Compound with Codeine **No. 3**, codeine phosphate* 32.4 mg. (gr. ½); **No. 4**, codeine phosphate* 64.8 mg. (gr. 1) *Warning—may be habit-forming. Each tablet also contains: aspirin gr. 3½, phenacetin gr. 2½, caffeine gr. ½.



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Respiratory tract

EMPIRIN[®] COMPOUND c CODEINE

#3, codeine phosphate* (32.4 mg.) gr. ½

#4, codeine phosphate* (64.8 mg.) gr. 1

The Role of the Detail Man

"I may be prejudiced, but I am very much in favor of the detail men I meet. Most of them are knowledgeable about the drugs they promote and can be a great help in acquainting me with new medication."

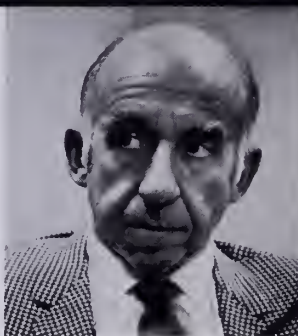
Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.

Dr. Willard Gobbell
Family Physician
Encino, California



Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School



"In the total picture of dealing with health problems in this country, there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likelihood on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Opinion
&
Dialogue

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility

of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone

in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love—they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and

thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.*, the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that informa-

tion must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

Pharmaceutical
Manufacturers Association
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Keeping things in balance...*

Antivert®/25 Tablets (25 mg. meclizine HCl)

***INDICATIONS.** Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation

has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children. Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy. See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

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when the eustachian tube has been adjudged to have returned to its normal functional state.

The second objective of treatment is directed at improving the condition of the eustachian tube and returning it to a normal functional state. The exact routine of the treatment depends entirely on the characteristics of the underlying problem. If the episode resulted as an acute process from barotrauma, further barotrauma should be avoided and the eustachian tube should be given an opportunity to return to normal. Systemic and local vasoconstrictors are helpful in this. The usual course of this problem runs from two to three weeks. Most cases clear up in this length of time on this regime.

Hyperplastic nasopharyngeal lymphoid tissue, especially that located in the Fossa of Rosenmüller, should be removed surgically to prevent further recurrence.

If the patient is an adult, and nonsuppurative otitis media occurs without apparent reason, or does not clear up promptly, the nasopharynx should be carefully examined by both the postnasal mirror and electric nasopharyngoscope. By these means, search for a carcinoma of the nasopharynx should be made, repeatedly, if necessary.

Sinusitis should be treated vigorously by standard methods. When it is cleared up, the edema and swelling of the eustachian tube usually subsides and the middle ear pressure is equalized by the eustachian tube.

Children with cleft palate often have recurring bouts of suppurative otitis media which may begin as nonsuppurative type. This problem is best corrected by the prolonged use of equalization tubes.

Although the use of antibiotics is helpful in clearing up bacterial infections, it has been postulated that some nonsuppurative otitis media has resulted from this therapy. Since antibiotics have come into common use, nonsuppurative otitis media has become a more commonly seen problem. The explanation for this lies in the fact that the antibiotic may sterilize the middle ear, but persistent edema of the eustachian tube may effectively prevent equalization of the middle ear pressure. The fluid then becomes inspissated and excessive amounts of mucus are secreted by the goblet cells of the middle ear mucosa.

The efficiency of antibiotic therapy is also subject to discussion. Some feel that the drying effect of the drug thickens and inspissates the fluid within the middle ear, thereby making equalization of pressure more difficult.

The use of antibiotics and antihistamines is both simple and, at best, a temporary measure. If the eustachian tube remains plugged, the most efficient therapy is the insertion of equalization tubes.

Most commonly the tympanic membrane heals up to become a normal drum membrane, but at times the process of healing results in either an atrophic

scar, or at times a tympanosclerotic patch in the tympanic membrane itself. At times, there is failure of the tympanic membrane to repair itself leaving a persistent perforation which is either central or marginal. These persistent perforations usually yield a simple stimulating measures.

Perhaps the most common complication is purulent otitis media arising in the ventilated middle ear. This often arises from water which gets into the ear from swimming, bathing or hair washing. Once purulent otitis is established, treatment with systemic antibiotics and topical antibiotic ear drops is begun. If this therapy is not effective in a short time, the equalization tubes should be removed. Often the removal of the equalization tubes, in addition to continued use of antibiotics, is adequate to clear up the infection. If the nonsuppurative otitis media recurs, the equalization tubes must be replaced after an appropriate interval of time.

If inadequately treated, if found in an especially susceptible individual, or if the infection is caused by a potentially virulent organism, mastoiditis may develop. If so, it must be treated as any acute or subacute mastoiditis.

Cholesteatoma may result as a complication of nonsuppurative otitis media or may arise from the implantation of epithelium within the middle ear by the process of insertion of the ventilation tube. Should the tube be located at the periphery of the tympanic membrane and a marginal perforation result, the migration of canal wall epithelium into the middle ear could produce a cholesteatoma. This must be treated as any cholesteatoma, from whatever source.¹⁰

CONCLUSION

Nonsuppurative otitis media is a common problem, especially in children, due to malfunction of the eustachian tube.

Although the morbidity is slight, the disability, due to hearing impairment, is great, and especially damaging to school age children.

Treatment is simple, either medical or surgical, and is aimed at restoring the eustachian tube to its normal functional state by equalizing the external ambient air pressure with that in the middle ear by means of medication or simple surgery, and the use of equalization tubes.

This disease should not be taken lightly, but should be treated aggressively to restore and maintain hearing at normal levels with minimal delay.

Equalization tubes provide satisfactory relief of the reduced middle ear pressure consequent upon obstruction of the eustachian tube.

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Gastrointestinal Bleeding Associated With Turner's Syndrome

A Case Report

JOHN W. TOWNE, M.D., F.A.C.S.*

In 1938, H. H. Turner first described a syndrome of infantilism, congenital webbed neck and cubitus valgus in the female.¹¹ This syndrome, now named after him, is characterized by ovarian insufficiency in the female, and may occur in the male.^{2,3} The karyotype reveals forty-five chromosomes with one chromosome being absent; thus an XO complement exists. On buccal smear, sex chromosome is absent in 80% of the cases.⁴ Mosaic forms such as XO/XX are common. In 1947, Lisser, et al, noted the association of this syndrome with gastrointestinal hemorrhage secondary to intestinal telangiectasia.⁶ Since that time, about twenty-one cases of Turner's syndrome with gastrointestinal hemorrhage have been reported.^{1,7,8,9,10,12} We would like to report an additional case in which the diagnosis of intestinal telangiectasia was made preoperatively.

CASE REPORT

K.P. is a twenty-one year old Caucasian female college student in whom Turner's syndrome has been well documented. One week prior to her admission to Thayer Hospital she was admitted to another hospital because of otherwise asymptomatic gastrointestinal bleeding of one week's duration. The bleeding was in the form of one large soft mahogany colored stool daily. She denied any nausea or vomiting, abdominal distress, or cramps. There had been no past history of previous episodes of gastrointestinal bleeding. At the other hospital, the hematocrit was 25%. Platelet count, prothrombin time, partial thromboplastin time, clotting and bleeding times were all within normal limits. Upper GI series, small bowel follow-through, and barium enema were done and thought to be within normal limits. After this negative work-up, she was then transferred to Thayer Hospital for further evaluation. On admission, she was a small Caucasian female with the typical webbed neck and increased carrying angle of the upper extremities seen in Turner's syndrome. She was forty-eight inches tall and weighed ninety-one pounds. She had small breasts and did have pubic hair, since she had been taking birth control pills for a number of years. Blood pressure was 100/60, temperature 98.6, pulse 76 and regular, and respirations were 20/min. No abdominal tenderness or masses were found. Rectal examination revealed mahogany colored stool which was guaiac-positive. Her hematocrit was 25.6, hemoglobin 8.2 grams, and the white cell differential was as follows: 48 polys, 47 lymphocytes, 4 monos, and 1 E.O. Platelet count was 244,000, and the white clotting time 15 minutes, bleeding time 1½ minutes, and PTT, 34.0 with a control of 30.0. Prothrombin time was 13.5 with a control of 11.0. SMA 12 laboratory profile was completely within normal limits.

During the night, following admission, the patient complained of feeling faint, her color became pale and her skin cold and clammy. Blood pressure dropped to 58/20mm. of mercury. She

was given two units of packed red blood cells in transfusion and the following morning her hematocrit was 32., hemoglobin was 10.5. It was felt that considering her diminutive stature, two units of packed red cells should have caused her blood count to be higher, and we suspected that she was still bleeding. Because of the known association of intestinal telangiectasias with Turner's syndrome, it was felt that that was the most likely etiology of her hemorrhage. The patient was then taken to surgery and underwent exploratory laparotomy. At celiotomy, intestinal telangiectasia was found, diffusely involving the small intestine. The middle of the small intestine extending almost to the ileocecal valve was most markedly involved. She was treated with resection of approximately one-half of the small intestine, thus removing the more severely involved areas of the bowel. End-to-end enteroenterostomy was carried out. She had an uncomplicated postoperative course and was discharged on the fifth day following surgery. Since discharge she is continuing to be stable, has had no further episodes of gastrointestinal bleeding.

DISCUSSION

Gastrointestinal bleeding secondary to intestinal telangiectasias is a fairly uncommon occurrence. Approximately 7% of patients with Turner's syndrome have gastrointestinal hemorrhage, and almost all of these, however, have intestinal telangiectasias or hemangiomas as the cause of their intestinal bleeding.^{5,6} Most present as melena and the usual preoperative diagnoses are duodenal ulcer, or Meckels' diverticulum. Schultz, in his review of the literature, found that in patients over the age of thirty the bleeding was intermittent and generally was self-limited, but in the younger patients there were three instances of life-threatening hemorrhage, and two deaths because of exsanguination.¹⁰ Demonstration of the lesions preoperatively has been difficult. Arteriography has been suggested, but the selective angiographic tests performed and reported have not successfully demonstrated telangiectasias.^{9,10} Hemangiomas if present may be visualized. Culdoscopy or laparoscopy may easily demonstrate the intestinal serosal lesions.

Treatment of this condition when significant gastrointestinal hemorrhage has occurred, we feel, should consist of resection of the bulk of the involved bowel when feasible. If both large and small bowel are diffusely involved, as is frequently the case, subtotal resection of the bowel should decrease the amount of chronic blood loss and decrease the need for periodic transfusions. Those patients with minor bleeding, and especially those over the age of thirty, may be treated conservative-

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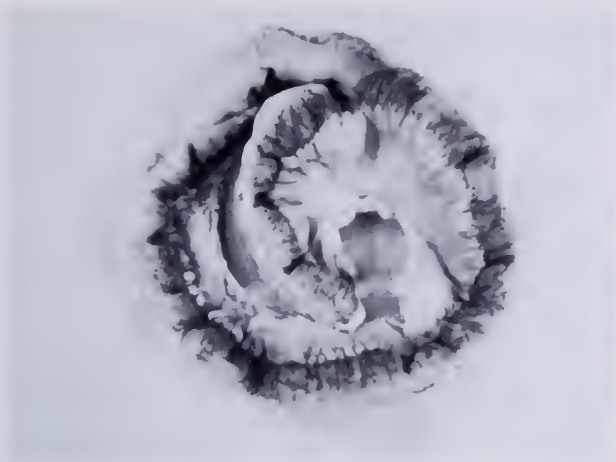


Fig. 1

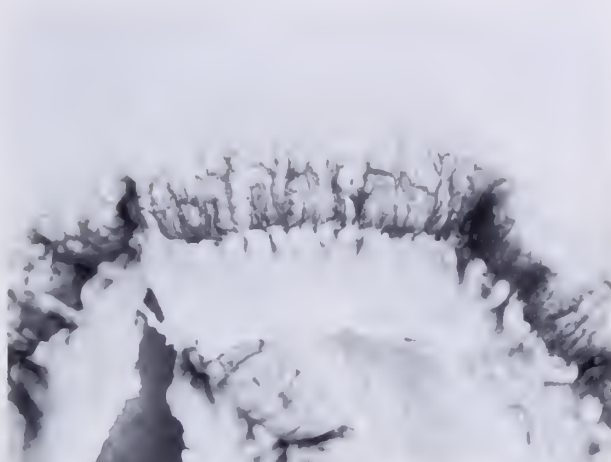


Fig. 2

ly, and may require occasional transfusions when followed over the years. Recurrence of intestinal bleeding is the rule rather than the exception following intestinal resection, but the amount of hemorrhage and need for transfusion is decreased.

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Continued from Page 35

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Extraosseous Manifestations of Plasma Cell Myeloma

EUGENE M. BEAUPRE, M.D.

As Dr. Waldenstrom points out in his classic monograph, *Diagnosis and Treatment of Multiple Myeloma*,¹ the name myeloma indicates that the disease should be regarded as present in the bone marrow. He further points out, however, "that extraosseous manifestations of the disease are not too uncommon, even as regards the clinical picture." The six case histories to be presented herein illustrate the many guises under which plasma cell myeloma may present (Cases 1 through 5), or the therapeutic dilemma that might be a prominent part of the clinical picture (Case 6). The cases also illustrate the wide spectrum of presenting complaints for which multiple myeloma must be considered in the differential diagnosis.

CASE REPORTS

Case 1. M.W., a 62-year-old woman, was admitted to the Neurosurgical Service of Thayer Hospital with an eight-month history of swelling of the right hand accompanied by nocturnal pain of the palm and wrist. Later she developed numbness of the palmar surfaces of the thumb, index finger, and middle finger. Pain was aggravated by use of the hand. Shortly before admission, she developed similar, but milder, symptoms of the left hand and wrist. Additionally, she had a five-year history of diabetes controlled by diet, and a one-year history of severe degenerative arthritis of the hips and spine for which she was receiving Indomethacin and Aspirin. By physical examination, she had a marked limp and walked with a cane. The right hand showed evidence of atrophy of the thenar eminence, hypesthesia of the palmar index finger, and weakness of the flexor of the distal phalanx of the index finger.

Electrodiagnostic studies showed delay of nerve conduction at the carpal tunnel bilaterally, worse on the right. Neurologic examination was otherwise normal. The patient was scheduled for surgical decompression of the right median nerve.

Preoperative laboratory data were as follows: Hemoglobin 10 gm.%, leukocyte count 6,050 per cubic millimeter, hematocrit 30%, platelet count 192,000 per cubic millimeter. Urine was free of protein. SMA-12 was normal except for a serum albumin of 3.1 gm.% and globulin of 9.7 mg.%. Because of the hyperglobulinemia, a diagnosis of multiple myeloma was suspected. Sternal bone marrow aspirate showed massive invasion by immature plasma cells. Serum protein electrophoresis showed an "M spike" in the beta globulin area. Metastatic bone survey showed diffuse, marked osteoarthritis. The only bony findings suspicious of myeloma were in the supracondylar portion of the right femur which showed mottling consistent with either myeloma or disuse atrophy.

The median nerve was successfully decompressed without complication, and therapy with Melphalan was begun. Four months later surgical decompression of the left median nerve was carried out uneventfully.

Comment: Of the various peripheral entrapment neuropathies, entrapment of the median nerve in the carpal tunnel is by far the most common. Of 73 patients with nerve entrapment reviewed by Cracchiolo and Marmor,² 53 had the carpal tunnel syndrome. Although Phalen,³ who saw 379 patients at the Cleveland Clinic from August 1, 1964 to January 1, 1969, minimizes the need for

searching for systemic diseases causing carpal tunnel syndrome, it is widely recognized that rheumatoid arthritis, acromegaly, tumors and cysts, myxedema, diabetes, and collagen vascular diseases may underlie the carpal tunnel syndrome. Of Cracchiolo's 73 cases of entrapment neuropathy, only one had multiple myeloma. And in this case, the carpal tunnel syndrome was only one of many manifestations of the disease. Cracchiolo stresses, however, that a number of systemic diseases can present with nerve entrapment as the chief complaint. In his series, this was true of two cases of rheumatoid arthritis, one of acromegaly, one of amyotrophic lateral sclerosis, and two of tumor. Thus, we should consider and search for possible underlying systemic disease when a diagnosis of carpal tunnel syndrome is made. The case presented above stresses the need for including multiple myeloma in the differential diagnosis.

Case 2. A.N., a 70-year-old white married man, was admitted to Thayer Hospital on January 11, 1973, for increasingly severe low back pain of three weeks' duration, complicated more recently by left anterolateral chest wall pain aggravated by inspiration. He had had viral pneumonia one year before and herpes zoster six months before admission.

Physical examination was "surprisingly unremarkable." He complained of upper lumbar spine pain when rising to a sitting position and of pain in the left anterolateral chest on deep inspiration. Physical examination of the chest was unrevealing, however. Chest x-ray showed a peripheral, rounded, soft tissue tumor invading the adjacent rib and mid-portion of the left lung (See Figs. 1 and 2).

"Primary tumor search" consisting of barium enema, intravenous urogram, upper gastrointestinal x-ray, and cholecystogram revealed no primary lesion, but there was a destructive lesion involving the first lumbar vertebra with only a small part of the vertebral body visible posteriorly. Tentative diagnosis was carcinoma of the lung with destruction of the adjacent rib and metastasis to the lumbar spine.

Hemoglobin was 12 mg.%, and leukocyte count 3,800 per cubic millimeter. Platelet count was 164,000 per cubic millimeter. Acid phosphatase was 1.7 units (normal 0.5 to 5.0 units). SMA-12 was normal except for a serum albumin of 3.1 gm.% and a globulin of 5.4 gm.%. There was no protein in the urine. Serum protein electrophoresis demonstrated a paraprotein peak in the beta-gamma region. Sternal bone marrow aspirate showed "a great predominance of plasma cells." A diagnosis of multiple myeloma was made, and cobalt therapy was given to the chest lesion and destructive spine lesion. Subsequently, he was treated with Phenylalanine Mustard and parenteral Testosterone Enanthate. He is virtually asymptomatic at present.

Comment: When one is confronted by a pulmonary parenchymal shadow complicated by erosion of an adjacent rib, one ordinarily thinks of carcinoma, primary or secondary, of the lung with pleural involvement. The clinical picture in this man was consistent with a diagnosis of peripheral bronchogenic carcinoma with metastatic disease to the first lumbar vertebra. This was the tentative diagnosis until the anemia and reversed A/G ratio were recognized as suggesting the possibility of multiple myeloma. Snapper, Turner, and Moscovitz, in their monograph, *Multiple Myeloma*,⁴ stressed that the roentgenographic appearance presented by this man was not uncommon in multiple myeloma. The lesions may be solitary suggesting primary bronchogenic carcinoma, or multiple suggesting metastatic carcinoma to lungs. Recognition of the possibility of such a diagnosis is important so that an unnecessary thoracotomy is



Fig. 1. Peripheral pulmonary mass with rib involvement in Case 2.



Fig. 2. Lesion of Case 2 after radiotherapy.

avoided. Furthermore, an intravenous urogram should not be done in a patient with multiple myeloma since dehydration in preparation for the procedure has resulted in renal shutdown.⁵

Case 3. F.K., a 69-year-old white married man, was admitted to Thayer Hospital February 13, 1972, because of swelling of the right breast of two weeks' duration. One year before admission he had "a bad fall." After that, he suffered from intermittent stiffness of the back, each episode consisting of one to two weeks' pain causing difficulty walking. At the time of admission, the pain radiated to the xiphoid area, and was aggravated by deep breathing. On admission, the pain was so severe that he was unable to sit upright.

By physical examination, he bent toward the right side because of pain. Blood pressure was 200/70, and pulse 120 and regular. There were no enlarged lymph nodes. The right breast was completely replaced by a huge, hard mass, fixed to the underlying muscles (See Fig. 3). There was dried, serous material around the nipple of the right breast. Left breast was normal. Liver was not enlarged. Admitting diagnosis was carcinoma of the right breast with probable skeletal metastases.

Hemoglobin was 10 gm.% and hematocrit 28%. Leukocyte count was 6,000 per cubic millimeter, and platelet count 183,000 per cubic millimeter. Skeletal survey revealed moderate osteoporosis with multiple compression fractures of the dorsal spine (See Fig. 4). Needle biopsy of the breast mass unexpectedly disclosed solid sheets of plasma cells varying in maturity. Serum albumin was 2.5 gm.% and globulin, 9.4 gm.%. There was Bence-Jones protein in the urine. The paraprotein migrated in the gamma region by serum protein electrophoresis, and was IgG by immuno electrophoresis.

Cobalt therapy was given to the breast mass and dorsal spine. The tumor was extremely radiosensitive, and had almost disappeared when 2400 rads had been administered. At the completion of the radiotherapy, the total protein had dropped from 11.9 gm.% to 7 gm.%, and he was much more comfortable. Systemic therapy using Phenylalanine Mustard, Prednisone,⁶ and Halotestin⁷ was begun.

He was readmitted to the hospital March 6, 1973, with signs of spinal cord compression and pancytopenia. He died March 18,

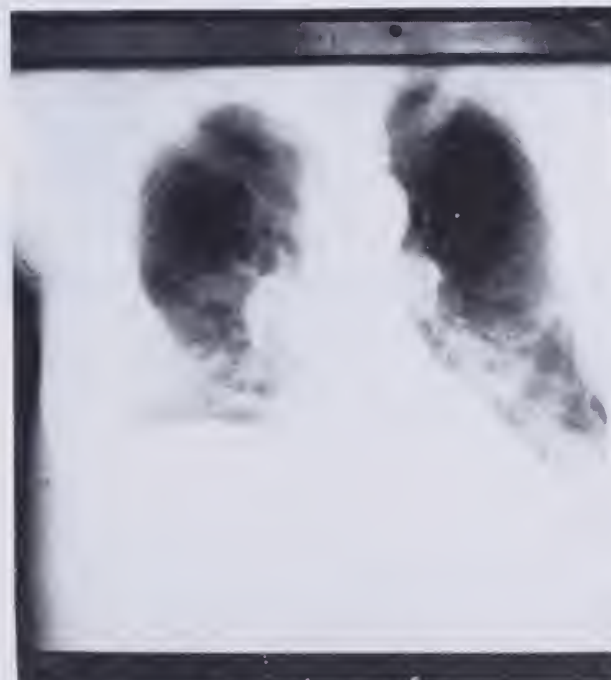
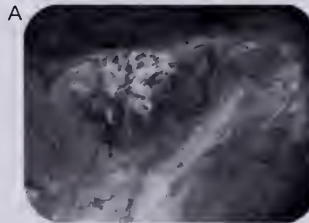
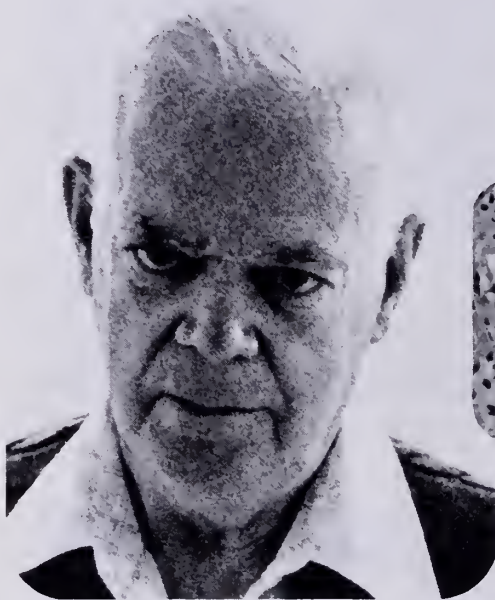


Fig. 3. Arrows demonstrate mass lesion of right male breast in Case 3.

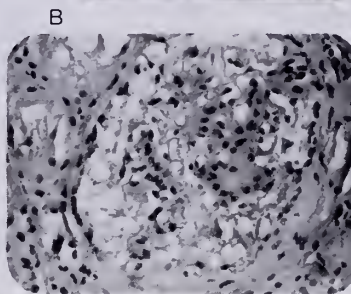
1973. Post mortem examination revealed widespread multiple myeloma.

Comment: Although clinically apparent soft tissue involvement by multiple myeloma is uncommon, up to 70 percent of cases have histologic evidence of plasma cell invasion of extra-skeletal tissues. Liver, spleen, lymph nodes, kidneys, and pul-

What's wrong with this "patient"?*



NOTE:
a variety of typical diagnostic
signs from three patients are
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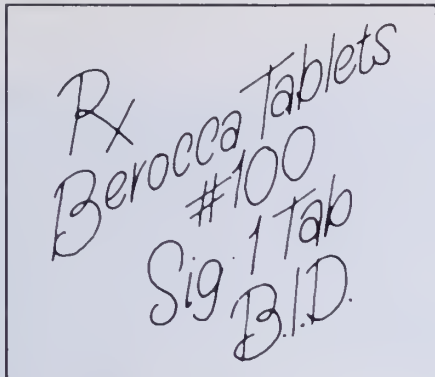
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DIAGNOSIS: Certain manifestations of diabetes mellitus are revealed in these photographs: (A) fundus shows neovascularization and marked retinal scarring (male, age 23); (B) biopsy of kidney shows early diabetic intercapillary glomerulosclerosis (male, age 35); (C) photos 1 & 2 show edema and loss of the plantar arch (female, age 59); (D) lateral x-ray (same patient) shows dropped arch and hypertrophic and destructive changes of tarsal and metatarsal joints (Charcot's arthropathy); (E) AP confirms hypertrophic and destructive changes in (D).

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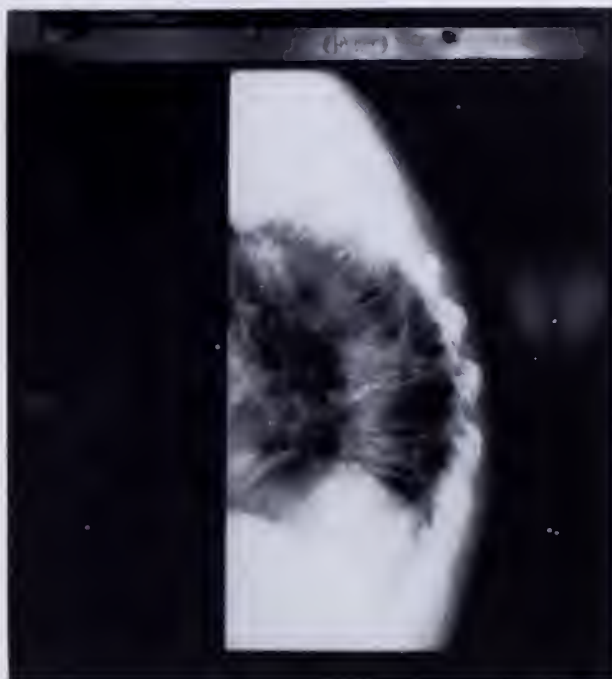


Fig. 4. Osteoporosis and multiple compression fractures in Case 3.

monary parenchyma are the soft tissues most often involved.⁶ With the exception of nasopharyngeal plasma cell myeloma, soft tissue involvement is seldom the dominant feature of the presenting clinical picture. In a review of 182 cases of extramedullary myeloma from the world literature and 38 new cases of plasma cell myeloma from the Mayo Clinic,⁶ no case of breast involvement by plasma cell tumors could be found.

Maeda⁷ describes recurrent myelomatous involvement of both breasts in a thirteen year old girl. In addition, she had multiple subcutaneous myelomatous deposits and widespread soft tissue and skeletal involvement. The author was able to find three other instances of breast involvement^{8,9,10} by multiple myeloma, all in women. Another instance of female breast involvement by myeloma was reported by Beevers.¹¹ She was an 81-year-old woman who also had multiple subcutaneous nodular deposits of plasma cells. The case described above seems to be the first reported instance of myelomatous involvement of the male breast.

Case 4. C.L.T., a 51-year-old white married man, was admitted to the Thayer Hospital on May 14, 1973. At that time, he was an obese, heavy smoking, ex-truck driver, admitted for increasingly severe dyspnea. For fifteen or twenty years, he had had exertional dyspnea with wheezing and chronic productive cough. Shortly before admission, he developed night sweats and purulent sputum. There was a strong family history of asthma. In the four years prior to this admission, his weight had increased from 225 to 260 pounds.

By physical examination, he was obese, apprehensive, short of breath, but not cyanotic. Blood pressure was 120/80, and heart was normal. There were generally decreased breath sounds and the expiratory phase of respiration was prolonged. There were rales in the right lower lobe.

Hemoglobin was 14.8 gm.%, and hematocrit 43.5%. Leukocyte count was 9,850 on admission, but rose to 20,400 by the fifth hospital day. There was no proteinuria. SMA-12 was normal (albumin 3.5 gm.% and globulin 3.7 gm.%). PO₂ was 51 millimeters of mercury, and PCO₂ was 40 millimeters of mercury. Chest x-ray showed consolidation of the right middle lobe (See Fig. 5), and pneumococcus was grown from the sputum. Pulmo-



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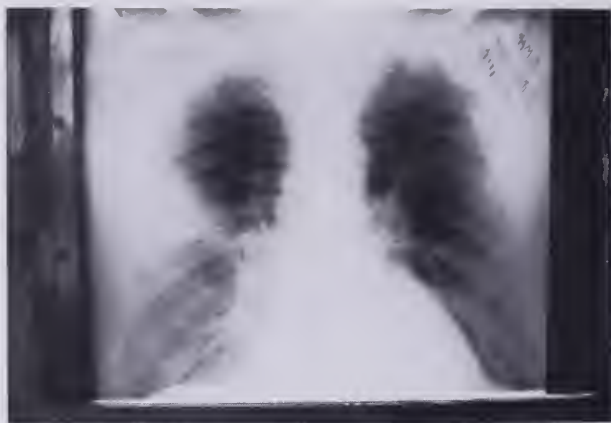


Fig. 5. Chest x-ray from Case 4 showing infiltrate in right middle and lower lung fields.



Fig. 6. Chest x-ray from Case 4 showing later pneumonitis in right upper lung.

nary function tests were consistent with moderately severe chronic obstructive lung disease.

He responded slowly to oxygen, a 1000 calorie diet, bronchodilators, Aminophyllin, and antibiotics.

He was readmitted October 7, 1973, with a temperature of 104.4 degrees Fahrenheit. Although no infiltrate was seen by chest x-ray, pneumococci were grown from three blood cultures, and he responded to parenteral Penicillin. Hemogram, except for the expected leukocytosis, and SMA-12 were again normal.

On October 19, 1974, he was admitted with a right upper lobe pneumonia (See Fig. 6). On this admission, his hemoglobin was 11.9 gm.% and hematocrit 34%. Leukocyte count was 9,100 per cubic millimeter, and platelet count, 159,000 per cubic millimeter. There was protein in the urine for the first time. Serum albumin was 4.1 gm.%, and globulin 4.6 gm.%. Because of the repeated infections, a serum protein electrophoresis was done. This showed a paraprotein migrating in the gamma region. The paraprotein was IgG by immuno electrophoresis. Bone marrow was grossly invaded by immature plasma cells, but there was considerable residual normal hematopoietic activity. Metastatic skeletal survey and polyphosphate bone scan revealed no evidence of bony disease.

Because the anemia was minimal and bone involvement inapparent by x-ray and scanning, it was decided to withhold specific antimyeloma therapy and treat with improved prophylactic respiratory care. In addition, all febrile disease will be treated promptly with appropriate antimicrobial therapy. Clinical course will be followed carefully, and antimyeloma therapy begun at the appropriate time.

Comment: As stated by Salmon et al,¹² bacterial infection is one of the leading causes of morbidity and mortality in patients with multiple myeloma. Ordinarily the infections become a problem at or after the time plasma cell myeloma is clinically obvious. Multiple myeloma, however, is one of the causes of impaired specific antibody synthesis,^{13,14} and, as this case illustrates, should be sought when repeated infections are a clinical problem despite the absence of bone pain and anemia. Patients with multiple myeloma have an almost specific susceptibility to pneumococcal pneumonia,¹³ and this is the most common cause of infection in such patients. Since the disease seems to be a cause of acquired agammaglobulinemia, one might consider the prophylactic use of gamma globulin. However, a controlled experiment by Salmon and his group¹² using 20 mg. of human gamma globulin every two weeks failed to show any benefit from the prophylactic use of this preparation. Therefore, early diagnosis and treatment of infection becomes an important part of the management of patients with plasma cell myeloma. Repeated infections may also be the presenting clinical picture as exemplified by this case, antedating clinically apparent bone disease.

Case 5. B.B., a 52-year-old white married woman, was admitted to Thayer Hospital for the first time November 10, 1972, for investigation of abdominal cramps. For the several weeks before admission, she had had epigastric distress occurring one to two hours after a meal. There was associated anorexia and occasional nausea and vomiting. Over this period of time, she had lost about ten pounds. She complained of rectal discomfort relieved by bowel movement, but with a sensation of incomplete emptying of the lower bowel. In addition, she had noted an abdominal mass just below and to the left of the umbilicus which had been present at least a year.

By past medical history, she had had a hysterectomy and repair of a recto-cystocele in 1960. An active peptic duodenal ulcer had been diagnosed in 1967. She had had a viral pneumonia with pleurisy in September 1971.

Her father died of cancer at the age of 79. Her mother, age 84, has temporal arteritis. Her husband died at the age of 47 of polycystic disease of the kidneys, and one daughter has the same disease.

By physical examination, she was a thin, but well-developed woman in no acute distress. There were no enlarged lymph nodes, and the liver and spleen were not enlarged by either percussion or palpation. There was a 3 cm. mass both visible and palpable just lateral to the umbilicus. It seemed to be fixed posteriorly.

By hemogram, she had a persistent pancytopenia with hemoglobin of 9.6 gm.%, leukocyte count of 2,100 with 37% segmented neutrophils, 13% bands, 40% lymphocytes, 9% monocytes, 1% metamyelocytes, and 3 nucleated red cells in the differential. Platelet count was 112,000 per cubic millimeter. Reticulocyte count was 1.2 percent, and direct and indirect Coombs tests were negative. Liver and spleen scan were normal. SMA-12 showed persistent elevation of the LDH in the 200 unit range (normal 30-120 units). Antinuclear antibodies were present in a titer of only 1:2. Serum protein electrophoresis was as follows: Albumin 3.4 gm.%, alpha 1 globulin 0.3 gm.%, alpha 2 globulin 0.7 gm.%, beta globulin 0.9 gm.%, gamma globulin 2.8 gm.%. There was no paraprotein. Immuno electrophoresis showed: IgA 400 mg.% (normal 167 to 409 mg.%), IgM 50 mg.% (normal 51 to 109 mg.%), IgG 1700 mg.% (normal 881 to 1519 mg.%). There was no Bence-Jones protein in the urine. Chest x-ray, skeletal survey, gastrointestinal and small bowel x-rays, cholecystogram, and barium enema were all within normal limits. Sigmoidoscopy was also negative.

On November 17, 1972, the abdomen was explored by a surgeon. The liver was described as normal size, but firmly nodular and slightly pale. Gallbladder was thin-walled and contained a single 12 mm. stone. The root of the small bowel and surrounding mesentery were involved by an "inflammatory process" with moderate edema, considerable induration, and multi-



Fig. 7. X-ray of left shoulder showing marked synovial thickening.



Fig. 8. X-ray of left wrist showing marked soft tissue swelling.

ple cysts up to 2 cm. in diameter. Sizable pieces were excised for pathologic examination. No discrete lymph nodes could be found. Spleen was removed and liver biopsied.

Pathologically the spleen showed acute congestion and fibrosis. Liver biopsy was felt to be normal. Biopsy of the mass showed dense aggregates of plasma cells forming small tumors. Plasma cells were described as well differentiated but not appearing to be an inflammatory reaction. Bone marrow aspiration from the sternum showed 4-5 percent plasma cells, but was not felt to be diagnostic of multiple myeloma.

The tissue specimens were sent to several pathologists. There was difference of opinion as to whether the biopsy specimens showed a bizarre plasma cell inflammatory response or myeloma or alpha heavy-chain disease. Subsequently, she has been admitted on three different occasions for investigation of her disease. Protein studies have been done by Dr. Ritchie of the Maine Medical Center. LDH, SGOT, SGPT, and alkaline phosphatase have become progressively more elevated, and a recent biopsy is consistent with chronic active hepatitis with early cirrhosis. Australia antigen has been absent from the blood. The most recent protein study has revealed IgG of 2,640 mg.% with three small "M bands." Up to present, these cannot be typed. Heavy chains have been sought both in the blood and in the urine but cannot be identified. The consensus of the many physicians who have been involved in the study of both the patient and the pathologic material is that she has malignant plasma cell disease with invasion of root of mesentery and persistent pancytopenia. Whether this will ultimately be plasma cell myeloma, heavy-chain disease, or some more atypical malignant plasma cell disease is yet to be determined.

Case 6. I.B., a 51-year-old white married woman, was admitted to Thayer Hospital for the first time on March 27, 1969, for

abdominal pain of two to three weeks' duration. In 1960, she had had a segmental colon resection with temporary colostomy for benign bowel disease. In 1955, she had had a total abdominal hysterectomy for excessive bleeding, and shortly thereafter had a right radical mastectomy for malignancy. Her father died in his eighties of carcinoma of the mouth, and a sister died of metastatic pancreatic carcinoma. The paternal grandmother and several aunts had all had "cancers." On admission, her hemoglobin was 13.2 gm.%. She had no protein in the urine, and her serum albumin was 4.5 gm.%, serum globulin 2.2 gm.%. She was felt to have psychophysiologic bowel disease and discharged.

April 3, 1970, she was readmitted with chills, fever, and occipital headaches. Hemoglobin was 13.8 gm.%, leukocyte count 6,150 per cubic millimeter, albumin 3.3 gm.%, and globulin 2.3 gm.%.

Two months later she was admitted to another hospital for recurrent fever. *E. Coli* was grown from her urine, and BUN was elevated to 33 mg.%. Anemia with a hemoglobin of 9.8 gm.% and proteinuria were both felt to be due to chronic infection and azotemia. One month later she was readmitted with nausea and vomiting. Blood pressure on admission was 190/100, but physical examination was otherwise unremarkable. During this admission, her anemia was investigated in more detail since her BUN had fallen to 14 gm.%. Serum protein electrophoresis showed a distinct paraprotein migrating in the gamma range by serum protein electrophoresis, and urine was positive for Bence-Jones protein on two occasions. Bone marrow showed infiltration by large numbers of plasma cells. Metastatic skeletal survey showed multiple, small, discrete areas of radiolucency in the skull consistent with metastatic disease or multiple myeloma. The remainder of the metastatic series showed no evidence of myelomatous involvement. Therapy was initiated with Phenylalanine Mustard

TABLE 1

Patient	Age	Sex	Presenting Symptoms	Albumin	Globulin	Hemoglobin	Leukocytes	Platelets	Paraprotein	Immunoglobulin
R.L.	65	M	Anemia, back pain.	2.4	7.9	6.8	7,350	134,000	Gamma	IgG
G.B.	65	F	Anemia, back pain.	2.7	6.9	10.6	4,450	166,000	Gamma	IgA
N.E.	85	F	Anemia, leg pain.	2.4	4.6	9.6	9,450	—	Beta-gamma	IgA
A.K.	61	F	Anemia, generalized pain.	1.9	9.1	7.8	8,550	220,000	Gamma	—
E.D.	70	F	Leg pain.	3.3	2.3	12.4	13,700	315,000	Urinary paraprotein	—
L.L.	76	F	Anemia, back pain.	2.7	7.0	6.4	4,500	—	Gamma	IgG
B.B.	36	F	Severe back pain.	3.5	1.5	12.4	7,900	167,000	Alpha 2	—
G.H.	61	M	Pain in ribs and legs.	2.9	9.6	12.0	4,400	295,000	Gamma	IgG
E.M.	85	F	Anemia	2.8	4.3	9.2	4,800	240,000	Gamma	—
A.T.	69	M	Anemia, shoulder pain.	2.3	6.9	10.6	6,400	255,000	Beta-gamma	IgA
A.B.	72	M	Painful skull mass.	3.3	4.4	14.0	9,800	426,000	Gamma	IgA
B.B.	57	M	Anemia, back pain.	2.4	10.0	9.0	3,500	123,000	Gamma	IgA

orally and Testosterone Enanthate intramuscularly. From this point on, she had multiple admissions for treatment of bone pain which responded to small palliative doses of radiotherapy. In addition, she had progressively severe azotemia and uremia.

An interesting complication of her disease was a migratory, inflammatory polyarthritis of obscure etiology. On February 20, 1972, she was admitted to Thayer Hospital for progressively severe, uncontrollable pain of the left shoulder. In addition she had weight loss, diffuse skin pigmentation, and extreme weakness. On that occasion, her hemoglobin was 9.6 gm.% and leukocyte count was 7,100. BUN was 93 mg.%. Creatinine was 8.3 mg.%. Because of uric acid elevation, a trial of Colchicine was given. This caused no relief of pain. Joint fluid was aspirated on several occasions; there were no uric acid crystals and cultures were sterile. Because of osteolytic lesions in the adjacent clavicle, a trial of cobalt therapy was given, but this also gave no relief from shoulder pain. Synovial biopsy was recommended but refused. In June 1972, she was admitted with nausea and vomiting and painful swelling of the right wrist. Swelling was diffuse, and the joint was tender (See Figs. 7 and 8). Range of motion was moderately limited. Pain in the left shoulder lessened slowly, but there was prominent synovial thickening so gross that it could be seen. In October 1972, she developed a painful effusion in the right knee. Subsequently, she developed typical median nerve entrapment in the carpal tunnels confirmed by nerve conduction time. Carpal tunnels were surgically decompressed which caused some relief of pain. She died four months later. At autopsy, she had diffuse involvement of joints by an amyloid-like tissue.

Comment: Arthritic symptoms are common with plasma cell myeloma, but most of them are caused by adjacent bone involvement by the myeloma itself. In a series of 46 cases from Hammersmith Hospital and Canadian Red Cross Memorial Hospital, Hamilton and Bywaters¹⁵ found eight instances of joint disease in six patients. Three were degenerative joint disease, two gout, two traumatic synovitis, and one para-amyloid infiltration of the carpal tunnels.

But uncommonly, as is true in this woman, a true arthritis complicates or antedates multiple myeloma. In two reported series,^{16,17} the inter-relationship between multiple myeloma, rheumatoid arthritis, and amyloidosis, especially of the joints, seems unclear. In some instances, well-documented rheumatoid arthritis terminates in multiple myeloma, while in others an atypical arthritis complicates multiple myeloma.

Zawadzki and Benedek¹⁸ subdivide such cases into "rheumatoid arthritis associated with monoclonal globulinopathy" and "dysproteinemic arthropathy." In the latter group, amyloid deposits have been found in some of the affected joints. The reported patient falls into the dysproteinemic arthropathy group since her joint symptoms arose after her multiple myeloma was moderately advanced and since she had amyloid infiltration of the joints.

DISCUSSION

Table 1 summarizes the remaining twelve patients

TABLE 2

PERIOD — 5 YEARS (1969-1973)	
Diagnosis	No. of Cases
Acute Leukemia	5
Chronic Lymphocytic Leukemia	5
Chronic Granulocytic Leukemia	6
Hodgkins Disease	20
Non-Hodgkins Lymphoma, i.e., Lymphosarcoma	14
Giant Follicular Lymphoma	1
Reticulum Cell Sarcoma	0
Grant Total	51

with plasma cell myeloma seen at Thayer Hospital over the last five-year period during which the six patients reported in detail were seen. The incidence of multiple myeloma is in the range of 2 to 3 per 100,000.¹⁹ Since Thayer Hospital's catchment area overlaps that of several other area hospitals, a reliable incidence figure is impossible. However, 3+ patients per year in one hospital in the Upper Kennebec Valley would seem to suggest a higher incidence than that reported above. It has also been reported that myeloma is seen with approximately the same frequency as Hodgkin's Disease and chronic lymphocytic leukemia.¹¹ The numbers of cases of malignant hemopoietic malignancies seen at Thayer Hospital over the same five-year period are listed in Table 2.

Patient A.B. seems to have a solitary plasmacytoma of the skull. But the majority of such patients, if followed long enough, develop disseminated myeloma. The other patients are typical examples of plasma cell myeloma with the expected anemia or bone pain.

Five of eighteen patients seen at Thayer Hospital over a five-year period presented with other than the typical bone pain and anemia complaints. Realizing that multiple myeloma may present with manifestations reflecting soft tissue involvement, amyloid deposition, or circulating antibody deficiency problems is important for several reasons. First, multiple myeloma is easily diagnosed once considered. One needs only a bone marrow specimen and appropriate electrophoretic studies of

blood and urine. A high index of suspicion would make unnecessary an expensive diagnostic workup, often with unnecessary exploratory surgery. Second, intravenous urography is potentially dangerous in multiple myeloma, a number of instances of renal shutdown having been reported.⁵ Early diagnosis of myeloma would obviate an IVP being done while looking for a primary tumor of origin. Last, multiple myeloma responds favorably to chemotherapeutic agents which should be used before pathologic fractures, with their considerable morbidity, appear.

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Approaches to the Evaluation of Physical Therapy Services

RICHARD T. CHAMBERLIN, M.D.

INTRODUCTION

The medical profession has been exploring new methods to best evaluate the quality of medical care. Although significant advances in techniques of review have been made, much remains to be done.¹ There is at least one definitive study, the results of which certainly appear to call for a note of caution in interpreting results of review efforts based on current accepted methodology.^{2,3} The problem becomes more complex when one undertakes to evaluate the services of some of the medical paraprofessional disciplines. This paper describes several efforts to evaluate physical therapy services in an acute general hospital which has an active continuing care (medical rehabilitation) service.

METHODS

The Thayer Hospital in Waterville, Maine is a one hundred and seventy-three-bed acute general medical surgical hospital. There has been an organized approach to providing for patients in need of rehabilitation medicine services throughout the periods described in these audits.⁴ The department — termed the Continuing Care Service — is under the direction of a physician and provides physical therapy, occupational therapy, social service, audiology, speech pathology, psychiatry, and mental health. From 1967 to 1973, the in-patient rehabilitation unit was a licensed distinct part Extended Care Facility. Since 1973, the long-term, in-patient rehabilitation needs have been provided under the guidelines promulgated in the Intermediary Manual Revision Transmittal #255, dated April 1972 from the Department of Health, Education, and Welfare — Social Security Administration.

The data for the audits to be described were derived from the various reports from the hospital's discharge abstract service, PAS-MAP, sponsored by the Commission on Professional Hospital Activities of Ann Arbor, Michigan. Each audit approach will be detailed and followed by comments pertinent to that particular study.

AUDIT APPROACH #1

The first approach was a simple descriptive listing of patients having a discharge diagnosis which might reasonably be expected to require physical therapy services in some instances. The table compares all those patients with a diagnosis of cerebrovascular disease in the year 1971 by whether or not they had

TABLE I

Studied	Total Sample (all pts. in same time period)	Those With P.T.	Those Without P.T.
1. Similarities			
Percentage male	65%	63%	64%
Diastolic B.P. over 100 mm	21%	47%	52%
Temperature over 100° F	5%	50%	50%
Pts. in ICU or CCU	13%	45%	54%
Pts. given Inhalation Rx	10%	50%	50%
Pts. given steroids	21%	47%	52%
2. Differences			
Average stay	8.1	45.0	12.9
Age differences			
Over 65	60%	43%	56%
Under 65	40%	25%	75%
Afebrile on admission			
Later fever	28%	43%	46%

physical therapy while in the hospital. In turn, those groups were compared with the gross aggregate data representing all patients seen in the hospital during the same time period (Table 1).

Comment. This approach did not help to solve the problem of evaluating physical therapy services. The similarities noted simply showed that patients with cerebrovascular disease were generally sicker than the average patient admitted during the same time period whether or not physical therapy was used and that those who did not have physical therapy were even sicker than those who did (more diastolic hypertension, more special care units used, more steroids used).

The differences noted in the table tended to confirm the above conclusion while also showing a marked difference in length of stay with those receiving physical therapy staying nearly three times as long as those who did not. There was no attempt to study comparative outcomes at that time. It also should be noted that in 1971 the hospital had an Extended Care Facility unit and many of the patients with cerebrovascular disease who did receive physical therapy were in the Extended Care Unit and, therefore, their length of stays lumped together with other length of stays tended to increase the overall average length of stay for those having services.

AUDIT APPROACH #2

The next approach was that of the consecutive case method of study. One hundred consecutive charts of patients receiving physical therapy were

TABLE 2

	Patients With P.T.	Patients Without P.T.
Total #	100	100
Average Age	55.5	45.8
% Males	40%	54%
# Transferred	12	1
# Deaths	6	6
Average L.O.S.	16.5	5.9
M.D. by Service		
Pediatrics	1	1
Medicine	31	33
Family Practice	0	3
Ophthalmology	1	5
Neurology	2	1
Surgery	27	29
ENT	2	8
Dental	0	2
Orthopedic	20	7
Urology	0	6
Neurosurgery, Psychiatry, Oncology, OBS-GYN	16	5

compared with one hundred who did not have physical therapy in 1973 (Table 2).

Comment. This approach, again, seemed helpful only in a descriptive sense. Patients receiving physical therapy tended to be older, more likely to be female, and stayed three times longer than those who did not have physical therapy. There seemed to be no clear-cut tendency to use physical therapy by any one of the services compared to any other except perhaps by the orthopedic service as might be expected.

AUDIT APPROACH #3

This approach provided a more in depth analysis of the physical therapy department. The method began with an analysis of the physical therapy order itself as it appeared in the records. The study ended with an attempt at analysis of the results of physical therapy as detailed in various progress notes and other documented information in the record. A worksheet was developed on which to record data pertaining to the physical therapy orders (Table 3).

An analysis based on these data is shown in Table 4.

Analysis of the results of this audit method would seem to substantiate the following conclusions. (1) The assumption made by many that physicians do not write their physical therapy orders is incorrect. However, the completeness of the orders is far from that which is desirable. Many times the hospital record's order sheet would simply read, "Physical therapy," or, "Send to physical therapy for backache." (2) The physician apparently does not understand or value a physical therapist's evaluation of a patient, at least as witnessed by the low rate at which such an evaluation was actually ordered. (3) Neither the physical therapist nor the physician documents response to physical therapy well at all

TABLE 3

WORKSHEET USED IN EVALUATION OF PHYSICAL THERAPY ORDERS

The Physical Therapy Order		Yes	No
I. Recording			
A. Order written by M.D.			
B. Order given by			
1. Voice			
2. Telephone			
II. Details of the Order			
A. Evaluation ordered			
1. If yes, was it done			
B. Modality named (heat, etc.)			
C. Modifier named (active, passive, etc.)			
D. Frequency mentioned			
E. Length of time mentioned			
F. Precautions detailed			
Physical Therapy Progress Notes			
		Complete	Incomplete
Initial Evaluation — where indicated			
Progress Note 1x/week			
Complication In Relation to P.T.			

as witnessed by the fact that almost one-fourth of the records reviewed contained no reference to whether the patient received benefit from such services or not.

AUDIT APPROACH #4

This approach was simply a listing of the statistical productivity of the physical therapy department in terms of unit of service rendered by the physical therapy service per unit of time (Table 5).

Comment. Since the size of the physical therapy department did not change in the years noted above — consisting of two registered physical therapists and two physical therapy aides, efficiency of producing services, at least by this statistical measurement, did improve slightly over the time studied. Not included of course in this method is the amount of time spent by the physical therapy personnel in such patient care related activities as attending weekly team conferences.

DISCUSSION

A review of the literature reveals that not much has been written with regards to the methodology of evaluating physical therapy services. One approach utilizes the systems analysis technique in such evaluation.⁵ In this report, it was helpful to list the specific objectives of physical therapy as a therapeutic modality as follows:

- (1) To restore to the highest level possible the physical functionings impaired by the disabling condition.
- (2) To deliver the physical therapy services in a manner which will most efficiently utilize the resources of the physical therapy system.
- (3) To continually improve the quality of these services through research and training in the field of physical therapy.

TABLE 4

<i>Item</i>	<i>Actual Number</i>	<i>Total Applicable</i>	<i>%</i>
1. Recording of P.T. order			
a. Written by M.D.	41	47	87%
b. Voice orders	3	47	6%
c. Telephone order	3	47	6%
2. Details of the order			
a. P.T. evaluation ordered	2	47	4%
b. Modality named (heat, exercise)	36	44	82%
c. Modifier named (active, passive)	18	36	50%
d. Frequency of treatment mentioned	15	47	32%
e. Duration of treatment noted	2	47	4%
f. Precautions detailed	6	46	13%
3. Details of P.T. response			
a. Evaluation done (actually seven were done — four of them with no specific order for evaluation)	3	3	100%
b. Progress notes once per week (one record had no P.T. sheet in record at all)	44	46	96%
c. Complication related to P.T.	0	46	0%
4. Effectiveness of P.T.			
a. This was very difficult to evaluate and will be summarized as follows: (1 record eliminated since no P.T. sheet found in record) — Eleven records were totally impossible to evaluate as no statements were made by either M.D. or P.T. as to whether P.T. helped or not. (24%) — Thirty-five records could be judged and were rated as follows:			
<i>Scale</i>	<i>Definition</i>	<i>Records</i>	<i>%</i>
0	No improvement	3	6%
1+	Slight	9	20%
2+	Moderate	13	28%
3+	Good	9	20%
4+	Excellent	1	2%
CNE	Could not evaluate	11	24%

TABLE 5

<i>Year</i>	<i># P.T. Man-hours</i>	<i># P.T. Treatments</i>	<i>Treatment Man-hour</i>
1971	7,930	11,065	1.40
1972	7,781	11,267	1.45
1973	7,937	11,969	1.51

On the basis of these three objectives, the following seven functions of physical therapy should be considered.

- (A) Patient care.
- (B) Research and training.
- (C) Administration.
- (D) Supportive services.
- (E) Transportation.
- (F) Communications.
- (G) Information.

Following the format of the approach by Kennedy, et al, the audit activity described above does not help describe physical therapy services well at all.

For instance, if one looks at the specific objectives of physical therapy as stated above, one can compare each of the audit methods used against how well it fulfills a study of each specific objective. Objective #1 was listed, "To restore to the highest level possible the physical functionings impaired by the disabling condition." Audit approaches #1, #2, and #4 do not meet any aspects of this objective at

all. One portion of the audit approach #3 — the effectiveness of physical therapy — only partly meets this objective. The rating scale for effectiveness is obviously too gross. Rarely in the physician's order or in the physical therapy response is an objective scale for measuring loss of physical function used. Physicians do not order physical therapy evaluation which might well document initial loss of function so that outcome could be compared to it. As for objective #2 — that is — to deliver the physical therapy services in a manner which will most efficiently utilize the resources of the physical therapy system, audit approaches #1 and #2 again do not meet this objective at all. Audit approach #3 indirectly measures efficiency and indicates a terribly low level of efficiency. If the physician's order does not include evaluation of the patient, specifics of modality or modifier, frequency, and duration — the physical therapist is left with no objective way to plan and deliver the services. This has to be inefficient. How many patients get physical therapy who do not need it? There is no way to answer the question. Audit approach #4 indirectly through statistics meets this objective and there does seem to be a slight increase in efficiency as measured by treatment per man-hour. Finally, as to objective #3 — to continually improve the quality of these services through research and training in the field of physical therapy, one finds very little or no research being done in

physical therapy departments in most community hospitals, and that training which is done is usually mostly limited to on-the-job training of physical therapy aides where a personnel problem exists. One should give credit, of course, here to the courses of continuing education that physical therapists do attend throughout the course of a year.

Finally, if one evaluates the audit activity undertaken against each of the functions of physical therapy listed by Kennedy, et al, one sees the following (Table 6).

TABLE 6

Function	Audit #1	Audit #2	Audit #3	Audit #4
Patient care	Defines population only	Defines population only	Direct measure	Indirect measure
Research & training	N/A *	N/A	N/A	N/A
Administration	N/A	N/A	N/A	Indirect measure
Supportive Services	N/A	N/A	N/A	N/A
Transportation	N/A	N/A	N/A	N/A
Communications	N/A	N/A	Direct	N/A
Information	N/A	N/A	Direct	N/A

*N/A = Not Applicable

Therefore, out of twenty-eight areas of measurement possible, the audit approaches taken directly measure only three and indirectly measure two more. Two more measures are descriptive measures only, but twenty-one functional areas are not measured at all.

CONCLUSIONS AND RECOMMENDATIONS

The analysis of physical therapy services as described in this article would seem to justify the following conclusions and recommendations.

1. The specificity of the initial order for physical therapy services should be improved and should include at least the following:

- A statement with regard to what functional loss has occurred. Where this is not known, physical therapy evaluation of functional loss should be ordered as part of the initial physical therapy order, and if not ordered, it should be done automatically by the physical therapist as part of the initial report.
- A statement should be made as to what specific goal of physical therapy is to be and, if not so stated, then the physical therapist should be allowed the professional judgement as to what the goals should be and as to when they are met in the course of therapy.
- The order should specify the type of physical therapy, the frequency of treatments, the duration of therapy, and what precautions, if any, should be taken during the course of therapy.

2. Some manner of functional rating scale should be adopted and used by all physicians and therapists within any given institution. There are many of

these such rating scales varying all the way from very specific numerical rating of individual muscle and muscle groups to more gross functional scales such as the PULSES Profile adapted from Moskowitz.⁶

3. Physical therapists should not be doing what nurses should be doing. After initial evaluation and recommendations are made, such routine things as range of motion and walking exercises should be performed under the supervision of nurses on the patient's general medical-surgical ward with assis-

tance and supervision from physical therapists only to the degree asked for by the nurses. Follow-up evaluations of progress, of course, should be done by the physical therapy department.

4. Programs of on-job training of physical therapy aides should be standardized in some fashion with a curriculum and not be left to the individual department heads totally.

5. A mechanism should be established to allow the physical therapist to discontinue services to those patients showing no further signs of recovery or benefit from their services. This is necessary to free physical therapy time to apply to those patients who have been shown in an objective evaluation to be likely to respond to therapy and who take more of the therapist's time.

6. There should be some regular audit of all active physical therapy cases to answer the very specific question — "Is there objective evidence of improvement or not?"

7. The continued problem of prompt and ease of communication between all members of the medical care team, but particularly between physicians and paraprofessionals should be more seriously studied and solved.

SUMMARY

This paper has described several attempts made to evaluate the effectiveness of physical therapy services in an acute general medical-surgical hospital. Comparison of the methods used against at least one accepted method from the literature was accomplished. Recommendations for improving the techniques of evaluation of physical therapy services are made.

Continued on Page 64

Diuretics

JOHN T. HARRINGTON, M.D.

Diuretics

Diuretics are agents which are designed to effect a negative sodium balance by inhibiting the renal tubular reabsorption of sodium. Their primary therapeutic usefulness is in patients with edema or ascites, both of which are pathologic increases in extracellular fluid volume. This brief review will focus on diuretics in common use at present, namely, thiazide diuretics, loop diuretics, and distal blocking agents. Extensive reviews (including a review of osmotic diuretics) can be found elsewhere.¹⁻⁴ The use of diuretics for non-edematous states (e.g., hypertension, acute renal failure, hypercalciuria, diabetes insipidus) will not be discussed.

Since the rational use of diuretic agents demands a thorough knowledge of normal salt and water metabolism, a review is in order. A typical 70 kg individual has an "exchangeable" body sodium content of approximately 3,000 mEq which is virtually confined to an extracellular fluid (ECF) volume comprising 20% of body weight and 33% of total body water. Given a normal glomerular filtration rate (GFR) of 180 L/d and a plasma sodium concentration of 140 mEq/L approximately 25,000 mEq of sodium are filtered daily, an amount eight times greater than the total body stores of sodium. In a normal individual who is ingesting an ordinary diet containing, for example, 100 mEq of sodium/day, a similar amount of sodium/day must be excreted in the urine in order to remain in sodium balance. It is thus clear that greater than 99% of the filtered sodium (all but 100 mEq of the 25,000 mEq filtered) must be reabsorbed by the renal tubule in order to maintain sodium balance.

This exquisite balance is achieved by sequential reabsorption of sodium along the nephron. In the proximal tubule, approximately 70-80% of the filtered sodium is actively reabsorbed in an isotonic

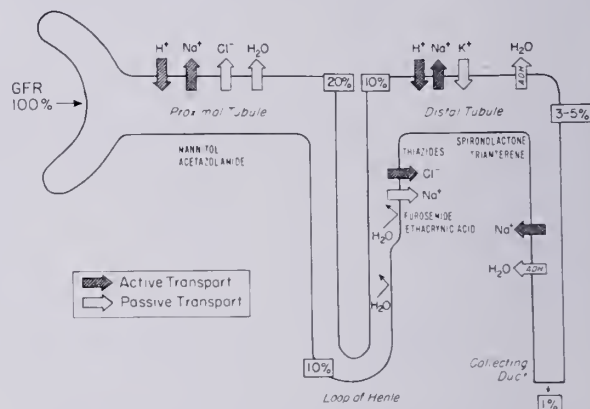


Fig. 1. Schematic drawing of nephron showing active or passive ion and water movement, percent of glomerular filtrate remaining in the various segments, and site of action of major diuretics.

fashion (see Fig. 1). It should be recalled that the bulk of bicarbonate reabsorption also occurs proximally via hydrogen ion secretion which requires the action of the enzyme, carbonic anhydrase. In the ascending limb of the loop of Henle approximately 10-20% of the filtered sodium is reabsorbed (approximately $\frac{3}{4}$ of the sodium delivered into the loop). At this site, however, it appears that chloride, not sodium, is actively reabsorbed. Solute reabsorption in the ascending limb differs from that in the proximal tubule in another important respect: namely, the tubular membrane is relatively impermeable to water so that as solute is removed, water remains behind, leaving the tubular fluid hypotonic or dilute, not isotonic as in the proximal nephron. Finally, the distal tubule and collecting duct recapture virtually all of the remaining 5% of the filtered sodium both by sodium chloride reabsorption and by cation-exchange ($Na^+ - K^+$; $Na^+ - H^+$). The rate of distal cation-exchange is governed by the rate of aldosterone secretion and by the rate of sodium delivered to the exchange sites.

In the normal individual whose dietary sodium intake is abruptly decreased from 100 mEq/day to 0 mEq/day, urinary sodium excretion rapidly decreases over the next few days to match sodium ingestion in order to maintain extra-cellular fluid volume. This renal regulation of sodium balance is accomplished by a series of factors comprising: 1) GFR; 2) aldosterone; 3) a volume control mechanism (probably not hormonal) which regulates

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sodium reabsorption in the proximal tubule. Thus, while the edematous patient may develop his or her state of positive sodium balance for a variety of reasons (cardiac, hepatic, renal), ultimately, sodium excretion must lag behind sodium ingestion (at least transiently) due to malfunction of one or more of the three factors described above. As noted earlier, diuretics are designed to correct this situation by increasing renal sodium excretion via inhibition of tubular sodium reabsorption.

Before proceeding to a discussion of the specific diuretic agents and their usage, it should be recalled that edema is *not* a primary diagnosis. Treatment should be specifically directed at the primary disease wherever possible, e.g., use of digitalis in congestive heart failure. Second, in many instances of edema, such as the mild physiologic edema of pregnancy or the edematous patient with hepatic precoma, diuretics may be specifically contraindicated. Third, the most common "side-effect" of diuretic therapy, volume depletion, is simply a consequence of the overzealous use of these potent drugs. The use of diuretics on alternate days, whenever feasible, is a simple and convenient way to reduce the likelihood of volume depletion. Finally, the use of several agents (in full dosage) which have their effect at different loci within the nephron may be required in order to achieve a successful diuresis.

Thiazide Diuretics

The benzothiadiazides were first synthesized in the late 1950's as an extension of studies on carbonic anhydrase inhibitors such as acetazolamide (Diamox). The latter class of agents is rarely used as diuretics at present because of their lack of potency. However, they are widely employed in the treatment of glaucoma and are useful in achieving alkalization of the urine. Chlorothiazide (Diuril) was the first member of the benzothiadiazides to be widely studied and is a model for the many analogs (including the nonthiazide, chlorthalidone, [Hygroton]) which have been produced subsequently.

Chlorothiazide is readily reabsorbed from the gastrointestinal tract. It achieves its maximal diuretic activity within 30-45 minutes after oral or intravenous administration and its effect disappears in approximately 6 hours. Thiazides are thought to inhibit sodium and chloride reabsorption in the early portion of the distal tubule (the "cortical diluting segment") though recent evidence suggests that thiazides may block active chloride reabsorption in the ascending limb of the loop of Henle (see Fig. 1). Maximum fractional sodium excretion observed when thiazides are studied under standardized laboratory conditions is between 5 and 8% of the filtered load. The specific chemical interaction between thiazide diuretics and the postulated "receptors" in the renal tubule is now known. The action of thiazide diuretics differs from other agents such

as the older mercurial diuretics and carbonic anhydrase inhibitors in that the renal effect is virtually independent of alterations in systemic acid-base equilibrium.

Since sodium reabsorption is blocked by thiazides "upstream" from the site of distal $\text{Na}^+ - \text{K}^+$ and $\text{Na}^+ - \text{H}^+$ exchange, it is not surprising that an accelerated rate of potassium and hydrogen ion excretion occurs. Moreover, the loss of sodium and the concomitant reduction in plasma and ECF volume lead to increased production of aldosterone via the renin-angiotensin mechanism, which will further accelerate distal cation-exchange. The increase in $\text{Na}^+ - \text{K}^+$ exchange leads to the well-known hypokalemia and potassium depletion observed in patients treated with diuretics. The increase in $\text{Na}^+ - \text{H}^+$ exchange and concomitant chloride depletion may produce metabolic alkalosis. Treatment of diuretic-induced hypochloremic metabolic alkalosis requires provision of sufficient chloride usually in the form of potassium chloride (approximately 40-60 mEq/day in 3 to 4 divided doses). Treatment of potassium depletion, when it occurs, can be accomplished by the administration of 40 to 60 mEq/day of 10% liquid potassium chloride, *not* potassium triplex, potassium bicarbonate (K-Lyte) or potassium gluconate (Kaon).⁵ The use of enteric-coated potassium supplements should be avoided because of the high incidence of distal jejunal or ileal ulcerations associated with their use. These untoward effects are probably due to high concentrations of potassium at the locus of dissolution of the tablets in the small intestine. Utilization of foods as sources of potassium is unreliable. Since the majority of patients do not develop clinically significant hypokalemia or potassium depletion, routine prescription of supplemental potassium is not required. The patient who is receiving concomitant digitalis therapy or the cirrhotic patient receiving diuretics needs closer follow-up evaluation so that hypokalemia and its consequences can be prevented.

Numerous complications of thiazide diuretics have been reported, including hyperglycemia, hyperuricemia, hypercalcemia, cholestatic hepatitis, and hypersensitivity (manifested by purpura, dermatitis, and necrotizing vasculitis). For reasons that are not entirely clear, hepatic coma appears to have been produced by the injudicious use of thiazide diuretics in patients with advanced hepatic disease.

Differences among the various thiazide derivatives are minor and a decision for one or another thiazide must therefore be based on differences in cost locally. 500 mg of chlorothiazide is equivalent to 50 mg of hydrochlorothiazide (HydroDiuril, Esidrix) and to 100 mg of chlorthalidone. Chlorothiazide (or an analog) can be given in a dose of 500-1500 mg/day (or its equivalent) in two divided doses.

Loop Diuretics

The two widely used loop diuretics, ethacrynic acid (Edecrin) and furosemide (Lasix), were both developed in the early 1960's and have subsequently attained a high level of clinical acceptance and utilization. Both are capable of producing a fractional sodium excretion of approximately 25% or more of the filtered sodium load (approximately 5 times as potent as chlorothiazide). Their potency, effectiveness when given orally, and relatively low rates of side effects have resulted in virtual abandonment of the use of the injectable organomercurial preparations. Although furosemide (a sulfonamide derivative) and ethacrynic acid (a phenoxyacetic acid derivative) are not structurally related, for all practical purposes, furosemide (40mg) and ethacrynic acid (50mg) can be considered interchangeable. The site of action of both is in the ascending limb of the loop of Henle, and thus both inhibit the diluting and concentrating mechanisms of the kidney (see Fig. 1). Both drugs are well absorbed orally, and have an onset of action within minutes when given intravenously. The peak effect is at 1-2 hours when given orally and at 30-45 minutes when given intravenously. Since the duration of action seldom exceeds 6-8 hours, in patients who are "resistant" to diuretic agents the dose can be doubled twice daily until a satisfactory response is observed or a maximum limit is reached. For instance, 40 mg of furosemide or 50 mg of ethacrynic acid can be given orally at 8:00 a.m.; if no response occurs within 6-8 hours (measured both in terms of urine output and weight loss), 2 tablets can be given at 4:00 p.m. the same day and if again no response, 4 tablets the following morning, etc. Although the usual maximum dose of both oral furosemide and ethacrynic acid is 200 mg, under carefully controlled hospital conditions as much as 4.0 gm of these drugs have been given daily. Urinary composition after the administration of these agents many contain as much as 150 mEq/L of sodium and chloride with little, if any, increase in bicarbonate excretion. As a result, contraction of ECF volume and hypochloremic metabolic alkalosis are quite common. Kaliuresis, due to increased delivery of sodium to distal exchange sites can reach levels five times that observed during the pre-drug control period. These agents remain effective in spite of extracellular fluid acid-base derangements. It should be obvious that if a patient is receiving a maximum dose of one of these agents, there is no rationale for the use of the other since both block sodium chloride reabsorption at the same site in the nephron. Since these agents block sodium reabsorption in the loop of Henle, where a significant percent of the filtered calcium load is reabsorbed, a marked increase in calcium excretion occurs with these drugs and this attribute has proved useful in the treatment of the hypercalcemic patient.⁶

Continued on Page 53

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdose or individual hypersensitivity, reactions similar to those after meperidine or morphine overdose may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy. Lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdose; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of 1/2 ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

SEARLE

Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Department, Box 5110,
Chicago, Illinois 60680

454 R

When diarrhea has his number...



Lomotil puts him back in the game.

Physicians and patients both want prompt control of the symptoms of diarrhea. A rapid, uncontrolled loss of fluids and electrolytes can cause a medical crisis, particularly in children, and in patients who are seriously ill, or in people who are badly undernourished.

Lomotil usually stops diarrhea promptly. This rapid action halts the emergency aspect of diarrhea

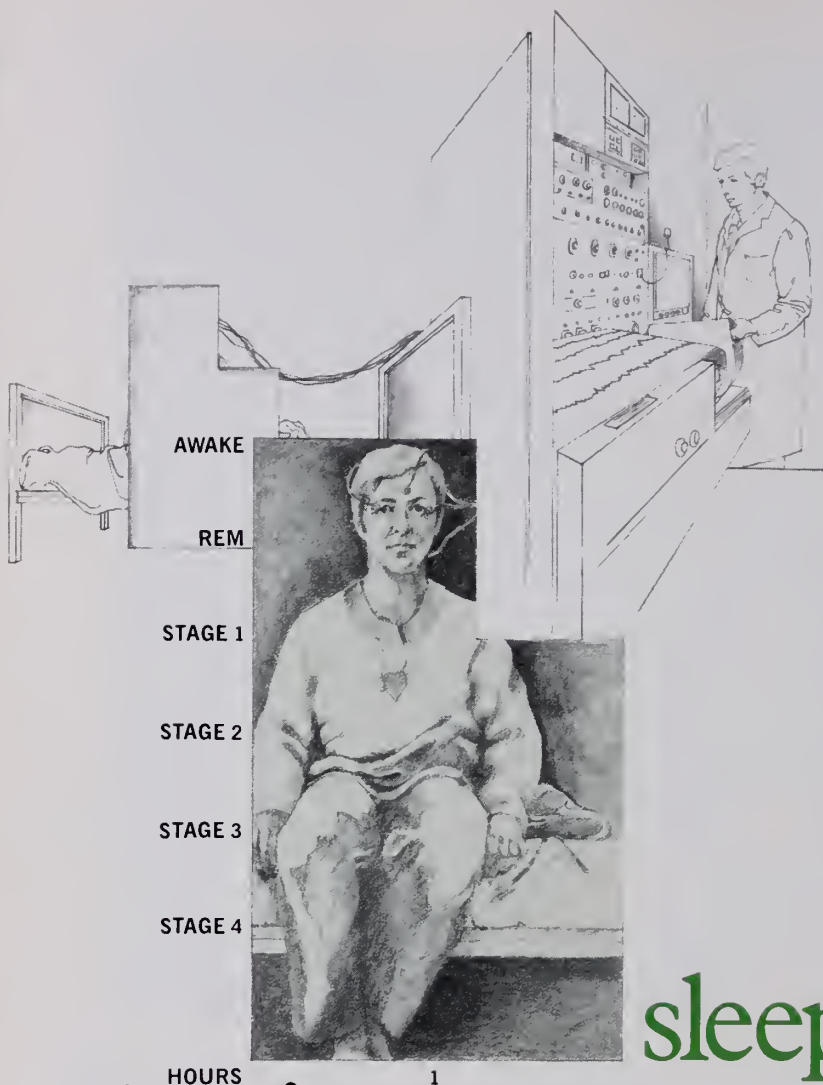
and is comforting and reassuring to the patient. Electrolyte and fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate antibiotic therapy should be given along with Lomotil.

Lomotil has few side effects, and those that do occur are generally mild.

Lomotil[®]
TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:
diphenoxylate hydrochloride 2.5 mg.
(Warning: May be habit forming)
atropine sulfate 0.025 mg.

Usually stops diarrhea promptly.

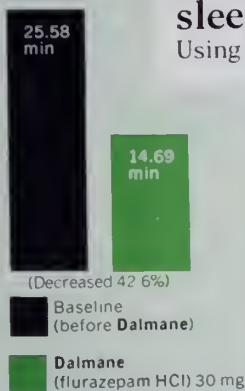


sleep
begins within
17 minutes, on average ...
an initial benefit of

Dalmane[®]
(flurazepam HCl) proved by a
22-night clinical study of insomnia patients
in the sleep research laboratory and at home¹

Three insomnia patients selected for difficulty falling asleep were administered Dalmane (flurazepam HCl) 30 mg for 14 consecutive nights. Placebo was given for four nights prior to and four nights after Dalmane. Physiologic tracings on Dalmane nights 1-3 showed sleep induction time averaged 13.90 minutes; on Dalmane nights 12-14, 18.80 minutes. Combined average for the 6 monitored drug nights was 16.35 minutes.¹

Average Time Required
to Fall Asleep (4 Studies,
16 Subjects²⁻⁵)



confirmed by clinical studies in four geographically separated sleep research laboratories²⁻⁵

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage²⁻⁵

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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4. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

when restful sleep
is indicated

Dalmane[®] (flurazepam HCl)

One 30-mg capsule h.s. — usual adult dosage
(15 mg may suffice in some patients).

One 15-mg capsule h.s. — initial dosage for
elderly or debilitated patients.

- induces sleep within 17 minutes, on average
- reduces nighttime awakenings
- sustains sleep 7 to 8 hours, on average, without repeating dosage

ROCHE

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities.

Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

KEEP THE HYPERTENSIVE PATIENT ON THERAPY KEEP THERAPY SIMPLE WITH **DYAZIDE**[®]

Trademark

Each capsule contains 50 mg. of Dyrenium[®] (brand of triamterene) and 25 mg. of hydrochlorothiazide.

Just 'Dyazide' once daily or twice daily
No inconvenient potassium supplements
Nor special K⁺ rich diets needed as a rule



Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

SK&F CO.
Carolina, P.R. 00630
Subsidiary of
SmithKline Corporation

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP

In contrast to thiazide diuretics, both of the loop diuretics remain effective even in patients whose GFR is as low as 5-10 ml/min. Doses higher than those conventionally administered (up to 500-1000 mgm/day) are usually required in these patients. While widely used, the efficacy of these agents in the management of the patient with acute oliguria remains controversial. I, personally, am skeptical of the reports which claim these drugs are effective in preventing or in treating established acute tubular necrosis. The necessity for their routine use in acute pulmonary edema is also not established.⁷

The conventional oral dose of furosemide is 40 to 200 mg/day, and of ethacrynic acid, 50 to 200 mg/day. Side-effects are comparable in both except that the unusual occurrence of deafness after intravenous administration appears to be slightly more common with ethacrynic acid. There may also be an increased incidence of gastrointestinal bleeding in patients receiving intravenous ethacrynic acid. In most hospitals, the cost of oral furosemide (40 mg) and of oral ethacrynic acid (50 mg) is virtually the same. The cost of intravenous furosemide is approximately one-half that of intravenous ethacrynic acid.

Distal-blocking agents (potassium-sparing diuretics)

There are two distinct types of diuretic agents which block sodium reabsorption at distal exchange sites. Spironolactone (Aldactone) competitively inhibits the action of aldosterone, while triamterene (Dyrenium), a pteridine derivative, directly blocks sodium reabsorption independently of aldosterone. For clinical purposes, however, these two drugs can be considered quite similar even though their fundamental mechanisms of action differ. The dose of spironolactone is 25 to 100 mg/day and of triamterene, 100-300 mg/day. Though side-effects are low with either agent, gynecomastia has been reported in a significant % of male patients who are receiving spironolactone. Both spironolactone and triamterene are only weakly diuretic; maximum fractional sodium excretion under standard laboratory conditions is approximately 2% (equal to or less than that of the carbonic anhydrase inhibitor, acetazolamide, which is no longer used as a diuretic). For this reason both drugs are usually employed in conjunction with a thiazide diuretic and/or

a loop diuretic. There is a slight further increase in sodium excretion under these circumstances but the major effect of distal blocking agents is inhibition of potassium excretion. The advantage of combined use of spironolactone or triamterene with a thiazide or loop diuretic is thus a decreased incidence of hypokalemia. However, there is a much higher incidence of hyperkalemia. The Boston Collaborative Drug Surveillance Program noted that 9% of hospitalized patients given spironolactone developed hyperkalemia.⁸ The frequency of hyperkalemia increased in those with azotemia or in those who were concurrently given potassium. On the basis of these and other data, distal blocking agents should not be used in patients with significant renal insufficiency (serum creatinine greater than 2.0 mgm%) and supplemental potassium therapy should be avoided. Fixed combinations of a thiazide diuretic and a distal-blocking agent are available and are widely used by physicians. They have the advantage of increasing patient compliance, but the disadvantage of the fixed drug ratio. It should also be recalled that the cost of triamterene to the patient is approximately two-thirds that of spironolactone, alone or in combination with a thiazide. For this reason when a distal blocking agent is used to further a diuresis and prevent hypokalemia, triamterene has a clear economic advantage.

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PSRO

The Pine Tree Organization for Professional Standards Review now anticipates that it will be approved for Conditional operation on or about April 1, 1975. In its draft plan for Conditional status, it established a time table for implementation of Admission Certification, Continued Stay Review and Medical Care Evaluation studies in Maine's acute care hospitals, delegating this responsibility wherever possible.

On November 29, 1974, new Utilization Review Regulations were published in the Federal Register requiring hospitals as a condition of participating in the Medicare and Medicaid Programs to install essentially the same type of review program as required by PSRO. These regulations, however, require an implementation date of February 1, 1975 unless waived.

At its meeting of December 18, 1974, the Pine Tree Organization's Board of Directors, Dr. Harry A. Bliss, Mr. William J. Carney, Dr. Richard T. Chamberlin, Mr. Douglas Dalrymple, Dr. Michael A. Longo, Dr. Donald K. McFadden, Dr. Thornton W. Merriam, Mr. Richard F. Nellson, Dr. J. Chase Rand, Dr. George E. Sullivan, and Dr. Herbert J. Wright, Jr. reached an agreement in principle that there should be only one Utilization Review system for Maine hospitals and Maine patients. That system should be the Professional Standards Review Organization's system.

PTO, through its hospital delegation responsibility, will share with all Maine's hospitals who wish it, the responsibility for effective Utilization Review.

Some hospitals are already moving toward implementing this new review process. We urge others to begin. Pine Tree Organization has available a model Utilization Review Plan developed by the Standards and Review Committee of PTO and approved by the state certifying agency. A draft Patient Care Coordinator Manual is available, as well as a suggested Patient Care Review form.

PTO's Standards and Review Committee, in conjunction with the State Peer Review Committee of the MMA and MOA, will soon publish Length of Stay norms for Maine hospitals based on Maine data. These may be used as regional norms as required by the new regulations.

The PTO's Standards and Review Committee will also be developing suggested criteria for admissions. Some Maine hospitals have started to develop their own. As we receive them, it is our intent to share them with all hospitals. There are, of course, already existing criteria available from various other sources as well.

It is the responsibility of the Pine Tree Organization's Standards and Review Committee to review all such criteria whether from national or local groups and adopt a set of criteria that express the needs of medical practice in this PSRO area.

The Board of Directors of the Pine Tree Organization invites all physicians licensed to practice in Maine to join the organization. A membership application follows. Please complete it and forward it to Pine Tree Organization for Professional Standards Review, Inc. c/o Richard T. Chamberlin, M.D., President, P.O. Box 706, 99 Western Avenue, Augusta, Maine 04330.

PINE TREE ORGANIZATION FOR PROFESSIONAL STANDARDS REVIEW, INC.

MEMBERSHIP APPLICATION

I, _____, presently admitted to practice medicine in the State of Maine, hereby apply for membership in the Pine Tree Organization for Professional Standards Review, Inc.

I understand that there are no financial commitments (i.e. dues) as a condition to my membership and that my membership shall continue as long as I am licensed to practice medicine in the State of Maine or until I voluntarily elect to resign. Resignation may be made at any time in writing directed to the Clerk of Pine Tree Organization for Professional Standards Review, Inc.

.....
Date

.....
Name

.....
Street

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City

.....
County



Putting out the fires of arthritic pain

Rheumatoid arthritis can sometimes spread like wildfire, with joint after joint going up inflamed. The usual onset is manifested by spotty joint involvement but an acute onset of symmetrical polyarthritis may be noted.^{1,2}

If aspirin fails, consider Butazolidin alka. Giving one capsule four times a day often provides prompt, pain-relieving, anti-inflammatory action to help restore joint mobility. The results you can get within a week can be maintained on as little as one or two capsules daily.

Serious side effects can occur. Select patients carefully (particularly the elderly) and follow them closely in line with the drug's precautions, warnings, contraindications and adverse reactions. For full details, please read the prescribing information. It's summarized on the back of this page.

Butazolidin® alka

Each capsule contains:
100 mg. phenylbutazone USP

100 mg. dried aluminum hydroxide gel USP
150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.



**Fire fighter
for arthritic
flare-ups.**

Butazolidin® alka

Each capsule contains:
100 mg. phenylbutazone USP
100 mg. dried aluminum hydroxide USP
150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.

Ragan, C.: The Clinical Picture of Rheumatoid Arthritis, in Arthritis, ed. 8, edited by J. L. Hollander and D. J. McCarthy, Jr., Philadelphia, Lea & Febiger, 1972, chap. 21, p. 335.

Geigy

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Substitute alka capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Rheumatoid arthritis, osteoarthritis, bursitis, acute gouty arthritis and rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia, history or presence of drug allergy; blood dyscrasias, renal, hepatic or cardiac dysfunction; hypertension, thyroid disease, systemic edema, stomatitis and salivary gland enlargement due to the drug, polymyalgia rheumatica and temporal arteritis, patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug, its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia, ulcerative stomatitis, salivary gland enlargement.

(B)98-146-070-J (10/71)

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
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DEAN H. FISHER, M.D.
COMMISSIONER

State of Maine

Department of Health and Welfare

Cervical Cancer Deaths in Maine 1968-1972

A Retrospective Case Study

PETER J. LEADLEY, M.D.,* SUZANNE MORRISON** and HOWARD YEATON‡

INTRODUCTION

From January 28 to April 26, 1974, the Bureau of Health conducted a study with the goal of determining the feasibility of planning a Statewide Cervical Cancer Screening Program in Maine. The Feasibility Study involved more accurate definition of the cervical cancer problem in Maine, as well as identification of resources presently available for screening. In the course of completing the Feasibility Study, death certificates of 228 women who died of cervical cancer in Maine between 1968 and 1972 were reviewed. The death certificate data, though helpful in providing information relating to age and geographic distribution of women who had died of cervical cancer, was inadequate to allow us to define certain other characteristics of the population group now at risk of dying of this disease.

In order to more accurately define the "high risk" population in Maine, the Maine Chapter of the American Cancer Society and the Maine Department of Health and Welfare co-sponsored a retrospective case study of 228 cervical cancer deaths between 1968 and 1972.

In conducting this study, we attempted to answer two major questions: (1) What characteristics define the "high risk" woman in Maine? (2) What is the level of contact with the medical care delivery system prior to the onset of cervical cancer? The importance of adequately defining a population group that is at high risk to a specific disease prior to implementation of services is obvious. Epidemiological studies are helpful in defining those groups of women who suffer the greatest frequency of cervi-

cal cancer (i.e., high risk groups). Studies concerning the epidemiology of cervical cancer are numerous and the results have been fairly consistent and well documented. Cervical cancer appears to be more frequent among:

- the poor
- non-whites
- non-Jews
- married women
- women who married early
- women who have had multiple pregnancies
- women with multiple sexual partners
- early and frequent sexual congress
- women whose consorts were uncircumcised
- those who contracted syphilis
- those who have unrepaired cervical lacerations¹

As the epidemiology of cervical cancer in Maine is undocumented, conclusions could only be drawn from the results of studies conducted elsewhere.

Our purpose in examining the level of medical care sought by women dying from cervical cancer prior to the onset of the disease is perhaps not so obvious. If this group of women sought routine medical care, including Pap tests, we would have to assume that the disease progressed so rapidly that a program designed to screen women would be ineffective in preventing death from disease. However, if this group of women did not seek routine medical care, we then would have to deal with their reasons for not doing so in order to design more effective educational and motivational methodologies necessary to bring these women to presented services.

METHODOLOGY

As mentioned previously, the population group of 228 women was selected from a five-year (1968-1972) review of death certificates. The death certificates revealed such preliminary data as

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LAST NAME FIRST MIDDLE HOSPITAL IDENTIFICATION NO.
 DATE OF DEATH RACE MARITAL STATUS
 AGE AT DEATH HOME RESIDENCE PHYSICIAN
 OCCUPATION Dx. AT DEATH

II. METHOD OF ENTRANCE INTO MEDICAL CARE DELIVERY SYSTEM

PRIVATE PHYSICIAN ☐ CLINIC ☐ EMERGENCY WARD ☐ OTHER ☐

III. FINANCIAL STATUS

- 1) HEALTH INSURANCE: _____
 2) YEARLY INCOME: SELF - _____ HUSBAND _____
 3) OCCUPATION OF HUSBAND: _____

IV. EDUCATION LEVEL

- 1) GRADE 8 ☐ 2) HIGH SCHOOL ☐ 3) COLLEGE ☐
 4) POST GRADUATE ☐ 5) NO FORMAL EDUCATION ☐ 6) GRADE _____ ☐

V. DIAGNOSIS STATUS AT LAST HOSPITALIZATION:

- 1) NOT DIAGNOSED PREVIOUSLY ☐ 2) DIAGNOSED PREVIOUSLY ☐
 DATE _____

Cervical Cytology Program
 Maine Bureau of Health

Patient's

Please respond by Aug. 9, 1974

Last Name First Middle Physician
 Home Residence Date of Death

- 1) Prior to the onset of cervical cancer was this patient one whom you would consider to be part of your practice? (ie: Would the patient probably have contacted you first for routine preventive care, minor self limited illnesses, etc., and/or did you maintain an active, on-going record on this patient?)

Yes ☐ No ☐ Unknown ☐

- 2) If the answer to (1) is "yes".

a) Did this patient seek regular preventive care (ie: physical checkups, routine immunizations, etc.)?

Yes ☐ No ☐ Unknown ☐

If "yes", approximately how frequently did this occur?

Every six months ☐

Every year ☐

About every two years ☐

Less than every two years but regular (ie: consistently every 4 years for 20 years etc.) ☐

Sporadically (unpredictably) ☐

- b) Did the patient see you only for acute problems (sore throats, vaginal discharge, stomach upsets, etc.)?

Yes ☐ No ☐ Unknown ☐

patient's name, date of death, age, occupation, place of death, residence and attending physician.

Of the 228 women, 165 died in hospitals, 34 died in nursing homes, 25 died at home and 4 died out of state.

DIAGNOSED BY:

- 3) SYMPTOMS ☐ 4) PAP SMEAR ☐ 5) BIOPSY ☐ 6) PHYSICAL EXAM ☐

VI. PREVIOUS MEDICAL CARE

- 1) NUMBER OF PHYSICIAN VISITS BEFORE DIAGNOSIS OF UTERINE/CERVICAL CANCER _____
 2) NUMBER OF PHYSICIAN VISITS AFTER DIAGNOSIS OF UTERINE/CERVICAL CANCER _____
 3) NUMBER OF PREVIOUS PHYSICAL EXAMINATIONS _____
 4) NUMBER OF PREVIOUS PAP SMEARS _____
 5) HISTORY OF PREVIOUS HOSPITALIZATIONS:

WHY WHEN HOW LONG

- 6) TIME LAPSE BETWEEN FIRST DIAGNOSIS OF CANCER AND PATIENT'S DEATH _____
 7) THERAPY USED AFTER DIAGNOSIS: DRUGS ☐ RADIATION ☐ OTHER ☐

VII. LIVING SETTING OF PATIENT

- 1) APARTMENT ☐ 2) HOUSE ☐ 3) TRAILER ☐ 4) NURSING HOME ☐
 5) NUMBER OF PERSONS LIVING WITH PATIENT _____
 6) RURAL ☐ URBAN ☐ SUBURBAN ☐

VIII. GENERAL COMMENTS RELEVANT TO INVOLVEMENT OF PATIENT WITH THE MEDICAL CARE DELIVERY SYSTEM PRIOR TO AND AFTER BEING DIAGNOSED AS A UTERINE/CERVICAL CANCER PATIENT.

APPENDIX II

- c) Was your contact with the patient only very sporadic (ie: last saw 15 years ago for delivery, saw once before many years ago for insurance exam, etc.)?

Yes ☐ No ☐ Unknown ☐

- 3) Was this patient not part of your practice and was referred for care for the cervical cancer.

Yes ☐ No ☐ Unknown ☐

If "yes" the referral was from:

Another physician in private practice ☐ Who _____

A hospital emergency room ☐ Which one _____

Other source ☐ Where? _____

- 4) Did this patient have regular routine pelvic exams prior to the onset of cervical cancer?

Yes ☐ No ☐ Unknown ☐

If "yes" were pap smears included in these?

Yes ☐ No ☐ Unknown ☐

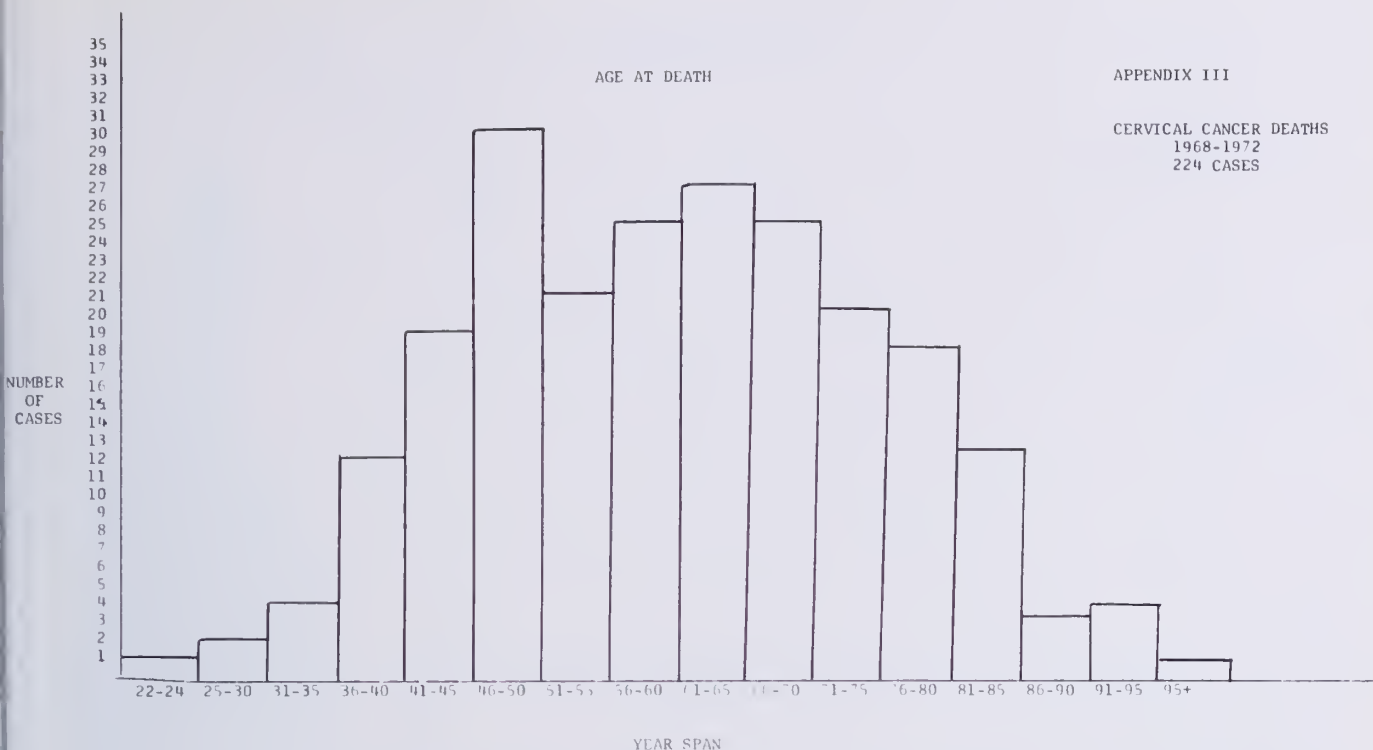
- 5) Did this patient have some other relationships to your practice not described above?

Yes ☐ No ☐ Unknown ☐

If "yes" please briefly describe.

This inquiry is to determine the nature and degree of contact that women presently dying of cervical cancer have with sources of medical care prior to the onset of their illness. The results will be used in determining the best strategy for a more-effective prevention program. Any ideas, comments, or suggestions you may have are welcome.

All nursing homes listed on the death certificates were contacted and asked if they had records of cervical cancer patients' previous hospitalizations. All hospital administrators were contacted and permission requested to review the medical records



of cervical cancer patients. Hospital visits for record review were scheduled on a regional basis.

A data form (Appendix I) was filled out from each woman's medical record. Information collected included (1) method of entrance into the medical care delivery system (i.e., private physician, emergency ward, clinic); (2) financial status (i.e., low — less than \$6,000 a year, middle — \$7,000-\$15,000 a year, high — \$15,000 or more a year); (3) educational level (i.e., grade school, high school, college, etc.); (4) diagnosis status at last hospitalization (i.e., whether diagnosed previously as cervical cancer or not); (5) method of diagnosis (i.e., Pap smear, biopsy, physical exam); (6) history of physician visits prior to the diagnosis of cervical cancer; (7) number of previous pelvic exams and Pap smears; (8) history of previous hospitalizations; (9) time lapse between first diagnosis and death; (10) living setting of patient. Initial record review suggested the advisability of noting cancer deaths among the patient's blood relatives, as well as the characteristics surrounding the diagnosis (e.g., presence of visible mass, symptoms that prompted the patient to seek medical attention and how these symptoms presented themselves). Other pertinent data was noted.

Additional patient data, as well as data on those women who died at home, was sought through the mechanism of a questionnaire (Appendix II) sent to physicians who attended cervical cancer patients. The questionnaire was oriented to specific medical care sought by the woman prior to the diagnosis of cervical cancer and included (1) regularity of past

physician visits; (2) nature of medical care sought (i.e., preventive, acute, sporadic, etc.); (3) regularity of past pelvic exams and Pap smears; (4) name of referring (family) physician, if any.

RESULTS

The original population group of 228 women was reduced to 186 because of the following factors: (1) missing or incomplete hospital records; (2) incomplete questionnaires (physician deceased or moved out of state); (3) four deaths occurred out of state and records were unavailable.

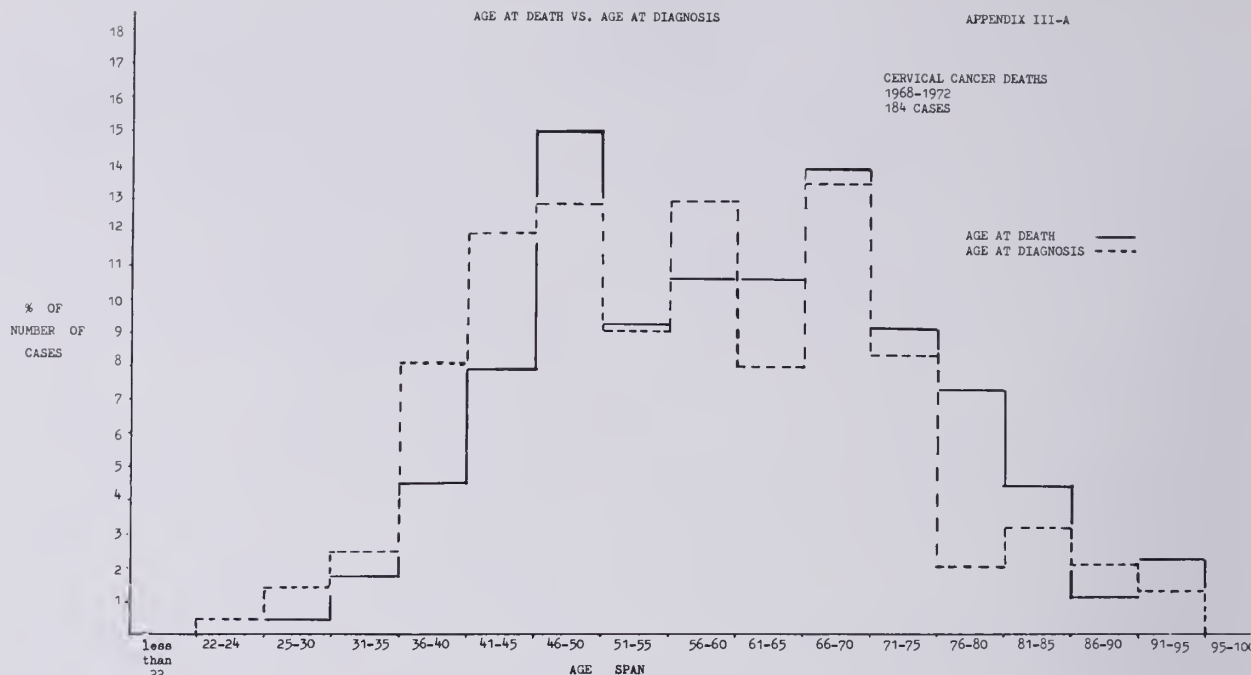
As a result of the above factors, 42 of the women fall into the category of unknowns. The women who died out of state have been eliminated from the study. The remaining 38 women who fall into the category of unknowns are discussed only in those categories where information was available from the death certificates (e.g., age of death, residence, etc.).

Age

The bar graph, Appendix III, shows a sharp rise in number of deaths at age 30 and a subsequent decline after the age of 70, with the mean age at death being 60. The two age groups displaying the highest number of deaths are those 46-50 and 61-65. Between 1968 and 1972, cervical cancer deaths accounted for over 5,000 years of life lost.

Occupation

The majority of women (68%) whose histories



were reviewed were housewives. Of the 32% who were employed, 27% were employed in non-professional positions (primarily laborers in mills, factories, etc.). As the majority of women were housewives, husband's occupation was noted as well. Of the men who were employed, the majority were employed in non-professional, non-technical positions and were primarily employed as laborers in mills and factories.

Financial Status

More than half (56.5%) of the women in the population group under study had incomes of less than \$6,000 a year. Of the 34% in the middle income level (\$7,000-\$15,000 annually), the majority had incomes on the lower end of the range. Three percent of the women were in the high income bracket. Sufficient data was not available on 6.5% of the group to accurately determine income level. The figures on income are hardly surprising in a state with a low annual per capita income (in 1970 — \$3,375) and a high percentage of persons, particularly in older age groups, living below poverty level.²

Marital Status

As marital status was listed on the death certificates, information was available on 224 of the women. Fifty-six percent of the women were married at the time of death, 32% were widowed, 9% divorced and 3% had never been married. Marriage certificates of 123 of these women were reviewed for more detailed information concerning age at first marriage and number of marriages. Of the 123 women, 34.9% had been married more than once. Data on age at first marriage was available for 100 of

these women. Forty-six percent were married before the age of 20. Average age at first marriage was 21. Of white women age 25 and above ever married in Maine, only 14% have been married more than once.³

Education

Of the 162 women on whom data was available, 59.7% had a high school education, 18.3% did not finish high school, 5.3% had some college education and 3.7% did not finish grade school or had otherwise limited educations. Of white women over the age of 25 in Maine, only 37.5% have completed high school, though a higher percentage (19.7%) have a college education than in our population group.⁴

Diagnosis and Entrance into Medical System

Seventy percent of the women made initial contact with the medical care delivery system through a private physician and were subsequently referred for further evaluation (e.g., from a physician in family practice to an oncologist, etc.) Twenty-five percent of the women, however, did not seek medical attention until vaginal bleeding, often hemorrhage or other acute and severe symptoms forced them into the emergency room of a hospital. Only 1% were referred to physicians or hospitals from clinics. Four percent of the women could not be accurately assigned to any of the above categories.

Sixty-three percent of the women whose records were reviewed were diagnosed by biopsy (usually following symptoms), while only 7% were first picked up by Pap smear. Twenty-one percent of the women who had a definitive smear classification (class III-V) had either a punch biopsy or cold con-

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176 CASES

ization to confirm the results of the Pap test. Though biopsy was utilized in the majority of cases for confirmation, initial diagnosis was frequently made on the basis of the physical exam itself. A fungating lesion or palpable mass was recorded in the medical records of 47.8% of the patients and was only definitively absent in the reports of 37%.

The major proportion (89.2%) of the women studied had been diagnosed at some time prior to their final hospitalization. However, 90.3% of the women had waited until vaginal bleeding, abdominal pain, drastic weight loss or other severe symptoms prompted them to seek attention. Only 6.5% of the women were definitely picked up by Pap smear before symptoms were grossly evident.

Medical records indicated that the majority of women in the 46-50 year age group, believing their symptoms to be associated with menopause, delayed two to three months in seeking medical attention. The 46-50 year age group is the time when the majority of women in the United States undergo menopause, and half of all women having a natural menopause do so by the age of 49.76. Women who have had regular menstrual cycles often experience a lighter, shorter flow with longer intervals between periods until menstruation ceases. Women who have had irregular menstrual periods usually ex-

perience even more irregular cycles until menstruation ceases.⁵ Although menopause is sometimes abrupt, it is usually a gradual process lasting over a period of years. The symptoms experienced by this group of women who died of cervical cancer did resemble those associated with menopause to the extent that they were unlike normal menses. However, the symptoms of vaginal bleeding discharge or spotting were primarily of longer, continuous duration (2 months-1 year) than those ordinarily associated with menopause.

The graph in Appendix IV indicates time lapse between diagnosis of cervical cancer and death for 97% of the cases examined. Seventy-two percent of the women died within 28 months of initial diagnosis of cancer. Only 7% (13 cases) of the women survived more than five years after diagnosis. Of these 13 cases, 7 survived ten years or longer. The graph in Appendix IVA presents a clearer representation of relative survival time for 176 of these women, median survival time being sixteen months after initial diagnosis. There was not any clear relationship between patient's age and relative survival time after initial diagnosis was made. Due to the variability in reporting the extent of involvement at initial diagnosis, no attempt has been made to correlate the degree of the lesion, i.e., Stage I-V, with the time

lapse period.

Medical Care History

The combination of data collected from hospital and physician records allowed for a reasonably accurate assessment of the medical care sought by the patient prior to the diagnosis of cancer. Only 8.6% of the women availed themselves of medical care on a regular, preventive basis. The majority, 51.6%, sought medical attention only for acute conditions (e.g., bad cold, broken leg, vaginal discharge, etc.), while 32.8% were seen by a physician only sporadically (e.g., delivery of a child, insurance exam, acute incident 20 years before). One woman had never been seen by a physician.

Twenty-six percent (49 women) had records of previous hospitalizations within five years of the diagnosis of cancer. Of the 49 women, 26.5% had pelvic exams and 14.3% had Pap smears as well as pelvic exams. In the majority of cases, the Pap smears were taken in response to symptoms. In New York State, the hospital code has been changed to include cytology as a routine part of admission procedure.

"An estimate of the potential reduction in cervical cancer deaths which might result in New York State if adult women received a routine 'Pap' test on admission to a hospital was recently developed through a survey of the hospital records of 427 women dying from cervical cancer. Twelve percent of these women had been hospitalized within 5 years prior to initial diagnosis without receiving a 'Pap' test or cervical biopsy. By applying this percentage to the average annual number of cervical cancer deaths, (it was) estimated that approximately 75 deaths attributed to cervical cancer might be prevented annually in New York through routine cytologic testing of all hospitalized women."⁶

Of the 186 women whose records we reviewed, 23% had been hospitalized within five years prior to the initial diagnosis of cervical cancer without receiving a Pap test or a cervical biopsy. By applying this percentage to the average annual number of deaths due to cervical cancer, approximately ten deaths might be prevented annually through cervical cancer casefinding in hospitals.

Pregnancy History

Of the 144 women for whom accurate obstetrical data was available, the average number of children per woman was four as compared to an average of 2.7 children/woman on a Statewide basis.⁷ Eleven percent of these women had had at least one miscarriage, 6.4% had had at least one aborted pregnancy, and 4.8% had had at least one cesarean section. For all of these cases, details behind these abnormal pregnancies were not listed. Only one woman had both an abortion and a cesarean section.

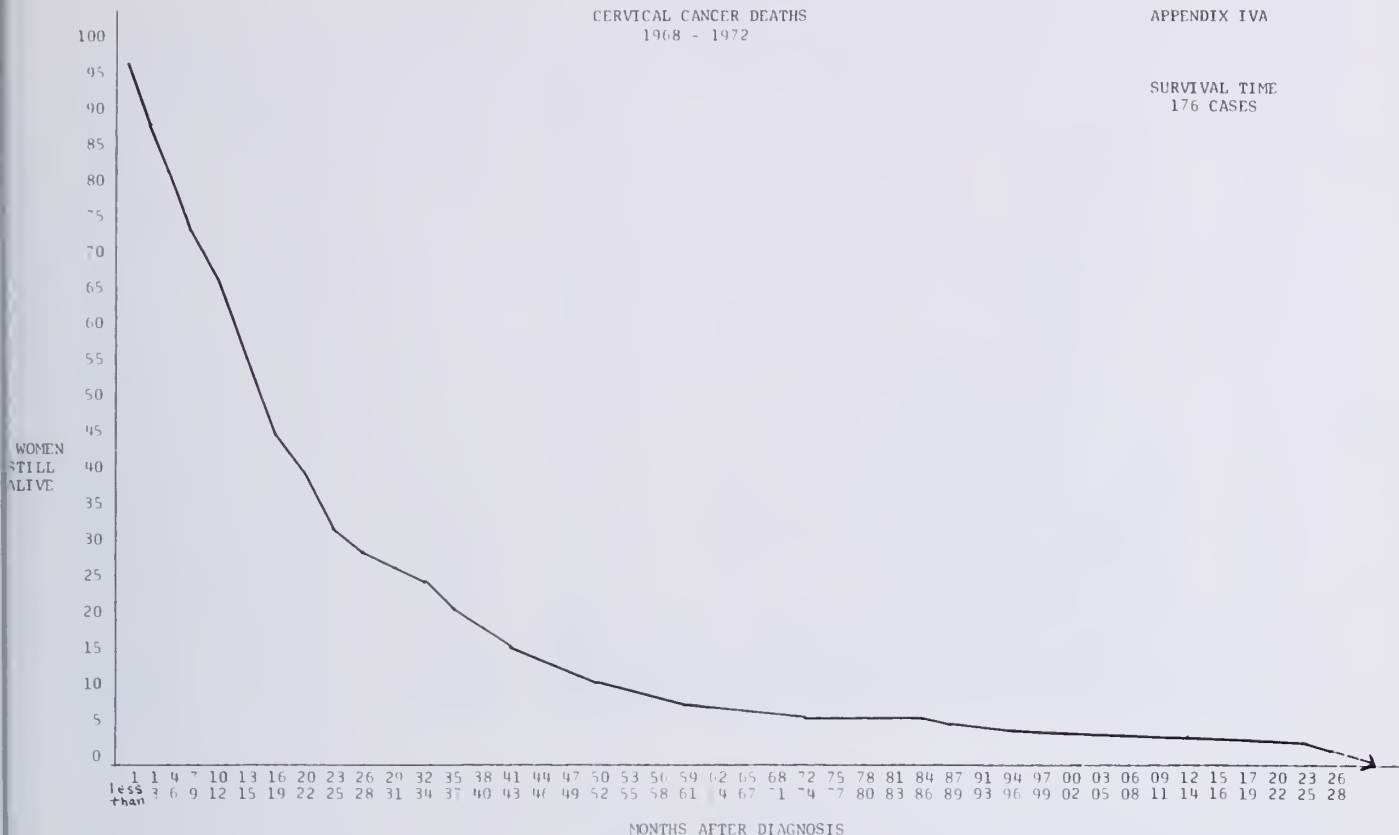
Special Features

Review of patients' records revealed three other characteristics with some consistency. 17.2% of the women had had supracervical hysterectomies or salpingo-oophorectomies in the past for non-cancerous conditions, ranging from excessive vaginal bleeding of unknown etiology to cystic or inflamed ovaries. In only one or two cases was routine follow-up examination sought. The vast majority of women presented themselves five to fifteen years later with fungating or eroded cervixes and vaginal bleeding of various durations. We find no references in the literature to gynecological surgery for benign disease and the later incidence of cervical cancer. Though no data is available on removal of the ovaries and a predisposition to cervical cancer some type of pathophysiology relating to cessation of ovarian hormone production may be indicated.

The family history of cancer was moderately well documented in a large number of records. 76.35% of the women were described as having no cancer among blood relatives, while 17.2% had reported cancer in parents, grandparents, siblings, blood related uncles and aunts. Though there is evidence to suggest that familial aggregation is present, cancer of the cervix as a site specific lesion is not thought to be inheritable.⁸

The third characteristic that appeared in the records of these women was a prior history of vaginal bleeding. Eight percent of these women experienced vaginal bleeding anywhere from one year to twenty-five years prior to the onset of cervical cancer. In all cases the women were found to be negative for cervical cancer at the time symptoms first appeared. The proportion of women in the general population who have such a complaint is estimated to be only about 4%.⁹ A study was made of the later occurrence of uterine cancer among 39,756 women who were examined between 1947 and 1953 in connection with the Lucas County, Ohio, uterine cancer program. Of the 29,320 women with negative Pap smears and genital cancer not found at the time of first examination, 20.8% were reported as having complaints and 79.2% were not reported as having complaints.

"The subsequent rate of occurrence of uterine cancer was higher among the women who reported complaints at the time of first examination than those who did not. During the first five years, the annual incidence rate of uterine cancer (including carcinoma in situ) was 2.76 per 1000 person-years for the complaint group and only 0.82 for the no complaint group, a ratio 3.37 to 1. The corresponding ratio was 4.18 to 1 for cancer of the corpus uteri, 3.27 to 1 for invasive carcinoma of the cervix uteri and 2.07 to 1 for carcinoma in situ of the cervix uteri. During the next five years, the annual incidence rate of uterine cancer (including carcinoma in situ) was 1.98 per



1000 person-years for the complaint group and 0.86 for the no complaint group, a ratio of 2.30 to 1.¹¹⁰

The conclusion drawn from this study is that women with a history of complaints are at higher risk to cervical cancer than women who do not have a history of such complaints.

In the population group under study, the percentage of women with a prior history of bleeding would be higher than the stated 8.0%, if those women who had had supracervical hysterectomies for bleeding of unknown etiology were included. The increase in the number of complete hysterectomies as opposed to supracervical hysterectomies for bleeding of unknown etiology will, in all probability, remove a percentage of women from the "at risk" group.

CONCLUSIONS

As mentioned in the introduction, our purpose in conducting this study was two-fold: (1) to identify those behavioral factors that characterize "high risk" women, and (2) to determine the level of medical care sought by this group of women prior to the onset of cervical cancer.

In general, behavioral factors related to the onset of cervical cancer identified among Maine women dying of the disease correspond to those identified in other studies. These factors include:

(1) Of the women who were employed, the majority were employed in non-skilled positions.

(2) The majority of women were married at least once.

(3) The percentage of women who were married more than once was higher among women dying of cervical cancer than among women in the general population.

(4) The majority of women had low annual income.

(5) The percentage of women with a prior history of complaints (i.e. bleeding, spotting, discharge) was higher among women dying of cervical cancer than among women in the general population.

There are a variety of factors identified in other epidemiological studies which we were unable to confirm in our study due to lack of data. Quite obviously, information regarding the sexual activity of these women was unavailable, and inferences could only be made based on the data regarding marriages. As far as obstetrical history is concerned, a large number of medical records contained no reference to number of births. In most of these cases, the women were over the age of 60 and the obstetrical history, when recorded, was noted as "unremarkable." Data regarding such factors as unrepaired cervical lacerations and age at first preg-

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nancy was unavailable in most cases. Other epidemiological studies remark on the low educational level of women at "high risk" to cervical cancer. In our population group, a higher percentage of women had completed high school than had women in the general population. All of the women who died of cervical cancer between 1968 and 1972 were white, which is not surprising in a state with a relatively small non-white population. This does not imply, however, that non-white women in Maine are at low risk to cervical cancer. The mortality rate from cervical cancer is higher for non-white women than for white women in Maine.¹¹

Perhaps what is most obvious, after reviewing the aggregate data in this study, is that the majority of women who died of cervical cancer between 1968 and 1972 could have been salvaged. This is not to imply that this group of women received a poor quality of medical care, but only that medical care was sought too late in most cases.

The effectiveness of the Pap test in detecting cervical cancer even in the non-invasive stage is well established. Although there is still some controversy regarding the progression of the disease, there is fairly strong evidence to support the premise that cervical cancer in the majority of cases follows a progressive course and that it may remain latent for long periods of time (as long as ten years).¹² Obviously, proof of the above theory is not possible, as it would involve allowing a known carcinoma to progress unchecked in a human patient.

As most of these women did not have regular Pap smears, we have no way of judging the length of time the disease progressed prior to the appearance of symptoms.

The data in Appendix IV and IVA indicate relative survival time between initial diagnosis of cancer and death (median time 16 months). The relatively short period of time between first diagnosis and death is not surprising. Chances of survival decrease with progression of the disease, and over half the women studied had a visible tumor on exam following symptoms.

Age at death corresponds well with national data on age incidence of cervical cancer, which shows a sharp rise around the age of 30 and a subsequent decline after the age of 70.¹³ Age at first diagnosis of cancer (Appendix IIIA) for this group of women indicates a shift to the left from age at death (Appendix III). If cervical cancer does indeed follow a progressive course, then the implication is that a rise in incidence may occur somewhat earlier among Maine women dying of the disease than is indicated by national data.

The majority of these women sought medical care on either an acute or sporadic basis. Of the small number of women who sought medical care on a routine basis, only 10 also had routine Pap smears. No data is available from medical records to indicate why the disease was not detected by the Pap test at an early stage. What may be indicated is either (1) a certain percentage of false negative

DATA TABLE 1

Occupation	Housewife 123/58%	Laborer 51/24%	Emergency Room 46/25%	Management- Clerk 20/9.4%	Other 14/6.6%	Unknown 4/2%	Total 212
Method of Entrance	Physician 131/70%			Clinic 2/1%		Unknown 7/4%	Total 186
Financial Status	Low 105/56.5%	Middle 64/34%		High 5/3%		Unknown 12/6.5%	Total 186
Education	Not Finish Grade School 7/3.7%	Not Finish High School 34/18.3%		High School 111/59.7%	College 10/5.3%	Unknown 24/13%	Total 186
Diagnosis Status	Not Diagnosed Before 16/8.6%	Diagnosed Before 166/89.2%				Unknown 4/2.2%	Total 186
Diagnosed By	Pap Smear 13/7%	Pap Smear/ Biopsy 39/21%		Biopsy 117/63%	Exam/ Surgery Autopsy 6/3%	Unknown 11/6%	Total 186
Pap Smear History	Routine 10/5.4%	Sporadic 26/14.1%	Rarely 2/1%	Never 16/8.6%	Recorded 123/66.1%	Unknown 9/4.8%	Total 186
Living Setting	Rural 78/37%	Urban 74/36%	Suburban 46/21%			Unknown 14/6%	Total 212
Case History	Acute 96/51.6%	Preventive 16/8.6%	Sporadic 61/32.8%	Never 1/5%		Unknown 12/6.5%	Total 186
Pregnancy History	Miscarriage 16/11%	Abortion 9/6.4%	Cesarean 7/4.8%			Unknown N/A	Total 146
Marriage History	Married 126/56%	Widowed 71/32%	Divorced 21/9%	Single 6/3%			Total 224
Number	One 83/68%	Two 32/26%	Three 5/4%			Unknown 3/2%	Total 123

DATA TABLE 2

	Yes	No	Unknown	Total
Previous Supracervical Hysterectomy or Salpingo-Oophorectomy	32/17.2%	144/77.4%	105/4%	186
Cancer Among Blood Relatives	32/17.2%	142/76.35%	12/6.45%	186
Diagnosis after Symptoms	168/90.3%	12/6.5%	6/3.2%	186
Visible Tumor on Exam Following Symptoms	89/47.8%	69/37.1%	28/15.1%	186

smears, or (2) an extremely rapid progression of disease.

Countless studies of the health care of Maine people substantiate the relationship between low annual income and poor health care (e.g., Fifteen Community Study, Indian Study, etc.). As the majority of the women whose histories we reviewed had low annual incomes, lack of adequate financial resources probably prevented many of them from seeking routine medical care prior to the onset of cancer. Surprisingly, the majority of these women (82.8%) were covered by medical insurance. Most medical insurance, unfortunately, does not cover the cost of preventive care. The fact that the majority of women had medical insurance and sought primarily acute or sporadic medical care leads to the supposition that the cost of illness may be considered "affordable" by a majority of people while the cost of staying well is not.

Ignorance, fear, and a strong process of denial on the part of many of these women were indicated by (1) refusal to have Pap tests, (2) linking of the symptoms of the disease with menopause even when

symptoms persisted for long periods of time, (3) refusal of adequate follow-up after initial diagnosis and treatment, and (4) ignoring symptoms until they became dramatic (e.g., major hemorrhage).

Knowledge regarding the Pap test and the cancer danger signal are fairly widespread. However, in many cases this knowledge is faulty. The findings from the study conducted by the American Cancer Society of women participating in the cervical cancer screening program in Ohio "... suggest that the 'danger signal' (i.e., bleeding) as now taught is effective in persuading women to be examined once but it appears to be less effective in persuading them to be re-examined."¹⁴ Unfortunately, too many women also believe that one negative Pap test is assurance against the future incidence of cervical cancer.

As adequate resources do not exist, at present, to screen all women for cervical cancer annually, regular screening of high risk women takes a high priority. However, not only is it necessary to provide services, but it is also necessary to design educational programs so that women will avail themselves

of presented services. If the "high risk" target population can be reached, a screening program would prevent mortality and should be implemented. The data in this study suggest the following:

Education

1. Education concerning the importance of the Pap test should begin at the high school level.
2. Men should be educated regarding the importance of the Pap test and the meaning of the cancer danger signal (i.e., bleeding) so that they may encourage their wives to seek medical attention. This might be best implemented through employers of non-skilled workers (e.g., mills, factories, etc.)
3. More definitive educational programs are necessary so that women can distinguish between the symptoms of menopause and those of cervical cancer.
4. Special efforts should be made to include post-menopausal women in screening programs. Individual educational efforts through visiting nurses, home health aides or family would be more effective with this age group than would mass media.
5. A reorientation toward preventive medical care is necessary. In line with this reorientation, consideration should be given to mandating that Pap tests be made reimbursable under health insurance.
6. Women who are identified as being at "high risk" (e.g., prior history of vaginal bleeding) should be adequately informed by a physician.

Screening

1. Women with a prior history of complaints (i.e., vaginal bleeding) should be "flagged" for screening. This group may be at least partially identifiable by selecting out those women who have had D & C's for bleeding of unknown etiology.

2. Women who have had supracervical hysterectomies or oophorectomies should be "flagged" for screening.
3. Routine Pap smear screening of hospital inpatients can be effective in reducing mortality from cervical cancer and is recommended.
4. Direct services as well as educational programs implemented through employers of non-skilled women (e.g., mills, factories) would reach a portion of the "high risk" population.
5. Regular screening of resident population groups (e.g., nursing homes, prisons, etc.) is recommended. Approximately 10% of the women in this study were members of resident population groups.

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Thayer Hospital, Waterville, Maine 04901



“STRESS”

“Stress” is the newest booklet in the Blue Cross Association Blue Print for Health series and is available to you or your patients through Maine Blue Cross and Blue Shield.

“Stress” is for the layman, although professionals will find it a source of many new and interesting facts. The subject is discussed in all its aspects: What stress is, how it was caused, how to overcome it and even what to do when nothing works.

It has been compiled under the professional guidance of Donald Oken, M.D., who is professor and chairman of the department of psychiatry at Upstate Medical Center, State University of New York at Syracuse.

“Stress” contains eleven articles by such well known authors as Lee Salk, Ph.D., whose pediatric accomplishments are known throughout the world; Gay Luce and Eric Peper who are involved in biofeedback research; Catherine Chilman, Ph.D., whose advice about stress in the home goes beyond theory because she is the mother of three; and others, including an industrial psychiatrist, a director of a gerontology center and a father-son team of physicians who challenge the reader to score the amount of stress at any given time from a point-value chart they originated. Not to be overlooked is one additional contributor who is not a scientist but she can “hold her own” when anyone mentions stress. She is Joan Rivers, the comedienne who thinks of life itself as one big stress reaction to be laughed at — and then overcome.

The booklet describes stress as it occurs to all age groups — infants, young children, adolescents and the elderly. Then “Stress” covers the environment as stress in the home and stress at work may differ but the causes are inter-related.

The concluding article in the booklet assumes that everyone at some time or other needs to relax but can't. The authors tell you how.

Quotes from “Stress”:

“The Chinese word for crisis is written by combining the symbols for the words ‘danger’ and ‘opportunity.’ Stress is just that: a danger and an opportunity; a friend and a foe. If you use it well, stress can be a good friend, indeed.”

Donald Oken, M.D.

Article: “Stress — Our Friend, Our Foe.”

“The child who is emotionally secure will find the

social and academic world interesting and challenging.”

Lee Salk, Ph.D.

Article: “Growing Up Mentally Fit.”

“For most youths, adolescence is indeed a possibility; that is to say, they belong to a world which emphasizes a prolonged childhood, a prolonged period of education and only a gradual entrance into the rights and responsibilities of adulthood.”

Robert Coles, M.D.

Article: “Mastering Adolescence.”

“Aging is a gift of the twentieth century to people who can learn to manage it and exploit it for what it can be.”

James E. Birren, Ph.D.

Article: “Weathering the Years.”

“The more you can accept that families have angry as well as loving feelings, that family members want to be free of each other as well as belong to each other, the less disenchanted you will be with family life.”

Catherine S. Chilman, Ph.D.

Article: “Home: Safe Harbor or Storm Center?”

“Establishing priorities and sticking to them is one good way to organize one's life to defeat stress.”

Ralph T. Collins, M.D.

Article: “Managing Stress on the Job.”

“Circumstances alter the impact and even the harm of a stressor . . . When the person behind you in the supermarket line gives you a shove, that's aggravation; when your grandchild sneaks up behind you for a surprise hug, it's a delight. Studies of stress must be able to account for the differences produced by these factors.”

Jerome E. Singer, Ph.D., David C. Glass, Ph.D.

Article: “Making Your World More Livable.”

“The routine of our lives is constantly being revised. We have to filter incoming stimuli, assign them priorities and try to fit them into our own way of life. If we refuse or are unable to deal with this input, our circuits may become overloaded with a massive life crisis and our systems are at great risk of breakdown in function.”

T. H. Holmes, M.D., T. S. Holmes, M.D.

Article: “How Change Can Make Us Ill.”

“The unpleasant psychological side effects of stress are not symptoms of current or future mental

Continued on Page 68

News, Notes and Announcements

Sixth Annual Surgical Symposium Maine Medical Center, Portland, Maine Friday and Saturday, March 7 and 8, 1975

All surgeons and other interested physicians are reminded of the MMC Surgical Symposium and cordially invited to send their reservations c/o Drs. Robert E. McAfee and Ferris S. Ray, Surgical Symposium Chairmen, MMC, Portland, Maine 04102.

This will be the first 1½ day symposium, and participating physicians are cordially invited to bring their wives.

Program Highlights

Isaac M. Webber Surgical Lecture:

"Surgical Trauma and Convalescence"

Francis D. Moore, M.D., Mosely Professor of Surgery,
Harvard Medical School, and Chief of Surgery,

Peter Bent Brigham Hospital

Presentations include "Unusual Cases of Surgical Trauma," "Present Your Problem Cases and X-Rays," "Surgical Updating," "Management of Surgical Trauma," and "Unusual Problem in Surgical Trauma." *Speakers* will include Drs. Dillihunt, Britton, Dibbins, Ray, Asali, Gibbons, McAfee, Phelps, Carroll, Drake, Provost, Pratt, Timothy, Clark, Goldfarb, Beach, Root, Hiebert, Leeber, and Caldwell.

Friday evening: Reception and Banquet at the Ramada Inn.

First Maine Biomedical Research Symposium

A symposium for clinical and research papers on the general topic of respiration will be held on March 14 and 15, 1975 at the Augusta Civic Center, Augusta, Maine. There will be sections related to clinical and marine and pharmacological and physiological aspects of respiration with a general section not specifically restricted to respiration. Continuing education accreditation has been approved by the AMA and the Maine Division, American Academy of Family Practice. For further details write: Chairman, Lucian J. Cuprak, Medical Research Service, Veterans Administration Center, Togus, Maine 04330.

"A Seminar in Emergency Medicine"

The Maine Medical Center and Tufts University School of Medicine announce "A Seminar in Emergency Medicine" to be held April 7-11, 1975, in Portland, Maine. Further information regarding registration may be obtained from Dr. Frank Lawrence at Maine Medical Center.

State of Maine Department of Health and Welfare Division of Child Health Clinic Schedule — 1975

Cardiac Clinics

Bangor — St. Joseph Hospital

9:00 a.m.: Mar. 14, Apr. 11, May 9, June 13, July 11, Aug. 8, Sept. 12, Oct. 10, Nov. 14, Dec. 12

Portland — Maine Medical Center

9:00 a.m.: Mar. 7, 14, 21, 28, Apr. 4, 11, 18, 25, May 2, 9, 16, 23, 30, June 6, 13, 20, 27, July 11, 18, 25, Aug. 1, 8, 15, 22, 29, Sept. 5, 12, 19, 26, Oct. 3, 10, 17, 24, 31, Nov. 7, 14, 21, Dec. 5, 12, 19

Orthopedic Clinics

Bangor — St. Joseph Hospital

9:00 a.m.: Mar. 27, Apr. 24, May 22, June 26, July 24, Aug. 28, Sept. 25, Oct. 23, Nov. 20, Dec. 18

Fort Kent — Northern Maine Medical Center

9:00 a.m.: Mar. 11, May 13, July 8, Sept. 9, Nov. 4

Houlton — Houlton Regional Hospital

10:00 a.m.: Mar. 10, May 12, July 7, Sept. 8, Nov. 3

Lewiston — Central Maine General Hospital

9:00 a.m.: Mar. 21, Apr. 18, May 16, June 20, July 18, Aug. 15, Sept. 19, Oct. 17, Nov. 21, Dec. 19

Presque Isle — A. R. Gould Memorial Hospital

9:00 a.m.: Mar. 12, May 14, July 9, Sept. 10, Nov. 5

Waterville — Thayer Hospital

Time scheduled by hospital: Mar. 3, Apr. 7, May 5, June 2, Sept. 8, Oct. 6, Nov. 10, Dec. 1

Cleft Palate Clinic

Portland — Maine Medical Center

10:00 a.m.: May 19, Sept. 15, Nov. 17

Cystic Fibrosis Clinics

Lewiston — Central Maine General Hospital

Time scheduled by hospital: Mar. 7, Apr. 4, May 2, June 6, July 11, Aug. 1, Sept. 5, Oct. 3, Nov. 7, Dec. 5

Portland — Maine Medical Center

Time scheduled by hospital: Mar. 18, Apr. 15, May 20, June 17, July 15, Aug. 19, Sept. 16, Oct. 21, Nov. 18, Dec. 16

Bangor — St. Joseph Hospital

Time scheduled by hospital: Mar. 18, Apr. 15, May 20, June 17, July 15, Aug. 19, Sept. 16, Oct. 21, Nov. 18, Dec. 16

History in the Making

W.A.M.M.A. is pleased to announce the formation of a new County Auxiliary. Lincoln-Sagadahoc Members-at-Large held a planning meeting at the home of Members-at-Large Chairman, Arlene Fichtner, January 8. An organizational meeting will be held February 3 at Bath Memorial Hospital.

Mrs. James Smith, chairman protem, will assist members in establishing a charter and electing their officers.

FOR THE DOCTOR'S WIFE

IF YOU LIVE IN A COUNTY WHERE THERE IS NO ORGANIZED AUXILIARY TO THE LOCAL MEDICAL SOCIETY, OR YOU FIND IT IMPOSSIBLE TO ATTEND REGULAR MEETINGS, JOIN THE AUXILIARY TO THE MAINE MEDICAL ASSOCIATION AS A MEMBER-AT-LARGE.

Even if you do not belong to a county auxiliary, you can become a member-at-large of your State Auxiliary and the Woman's Auxiliary to the American Medical Association. The medical profession needs your support and interest. As a member of this organization, it is your privilege to assist the medical profession in its program for the advancement of medicine and public health, and to serve in promotion of health education in your community.

The annual dues you pay (\$8) benefit everyone. They pay for:

- MD'S WIFE (National magazine)
- Direct Line Newsletter
- Operational expenses (including headquarters office, convention, conference and workshop expenses)
- Printing and distribution of Package Programs and health education aids
- Loans to medical students and nurses
- Scholarships
- Contributions to the American Medical Association Education and Research Foundation

Please be assured that we are interested in your personal participation in county, State and national auxiliary programs and not just your financial support. Contact your nearest local group as soon as possible and enjoy the friendship to which your membership entitles you, and contact me for enrollment.

MRS. PAUL A. FICHTNER
Chairman, Members-at-Large
Woman's Auxiliary, M.M.A.
Woolwich, Maine 04579

County Society Notes

PENOBSCOT

The October 1974 meeting of the Penobscot County Medical Society was held on October 15, 1974 at the Heritage Motor Inn, in Millinocket, Maine, with a large group in attendance.

The meeting was opened by the President, Dr. David Sensenig. The minutes of the annual meeting which took place in May 1974 were read and approved.

Applications for membership into the Penobscot County Medical Society were received from Drs. H. Clement Jurgeleit, John F. Adams, Jr. and Donald G. Metzger. All applications were reviewed by the Executive Council and approved. The applications were then voted upon and approved unanimously by the membership.

There was no old business.

Under new business, there was nothing to come before the membership for discussion or action. As a comment, Dr. George W. Wood, III acknowledged the fine dinner and accommodations of the evening which were planned by the members from Millinocket.

The speaker of the evening, Dr. Russell C. Briggs, of the Department of Nuclear Medicine at the Maine Medical Center, Portland, Maine, was introduced. His topic "A Peek Under the Mushroom Cloud" recounted the history of scanning in nuclear medicine and described the newer techniques available in the field. Recent advances in radioactive scanning, as well as the future direction which scanning might take, was highlighted by Dr. Briggs. The presentation was most informative and helpful to all who were privileged to hear it. A discussion period followed the formal presentation. As there was no further business, the meeting was adjourned.

PHILIP G. HUNTER, M.D., *Secretary*

CUMBERLAND

The 389th meeting of the Cumberland County Medical Society was held at the Stage Coach Restaurant in South Portland, Maine at 6:00 p.m., October 17, 1974. Ninety-three members and guests were in attendance. Following a well attended social hour, an excellent dinner was served. The steak was considered very good and the service very slow.

The meeting was called to order by the President, Dr. Stanley B. Sylvester, at 8:35 p.m. Three guests were introduced. They are Mr. Dalrymple from the Union Mutual Life Insurance Company, Dr. Dibbins (recently arrived pediatric surgeon) and Dr. Robert Sylvester who is now doing rheumatology in Portland.

Applications were then presented to the membership for first reading: Drs. Larry Anderson, Richard Anderson, George Morton, Robert Sylvester and Caroline Dickson, all for junior membership. These applications have been referred to the Executive Committee and will be brought back at a subsequent meeting for final vote.

In addition, Dr. Aldo Llorente of Brunswick asked permission to transfer to the Lincoln-Sagadahoc County Medical Society. This was approved.

The names of the following members were presented for honorary membership: Drs. William L. Casey, John J. Lappin, Philip H. McCrum and Alice A.S. Whittier.

Drs. Paul V. Davis, John R. Lincoln, Norman E. Dyhrberg, K. Alexander Laughlin, John B. Titherington, Donald F. Marshall, John V. Ward, Andrew Melkis and Nina Rubins were all proposed for affiliate membership.

Drs. Alvin A. Morrison and Roderick L. Huntress are now eligible for senior membership.

Drs. Hugh M. Phelps, Anthony F. Salvo, Michael L. Shuman, Charles F. Thurber, Louis E. Rosenthal continue as junior members while Drs. Claude A. Burnett, Jr., Clifford W. Gates, David M. Iszard and Richard B. Stephenson are service members. The above special membership categories were approved by the Society.

The Auxiliary of the Cumberland County Medical Society has

asked for \$180 as a contribution toward the tasting supper tomorrow night. The Executive Committee has approved the \$100 donation, but is prohibited by the Bylaws from increasing this amount. It was pointed out that the appropriation of monies in excess of this requires one month's notice and must be brought up at the following meeting. However, since \$100 has already been appropriated, it is possible for the Executive Committee to add \$80 to this at the time of our next meeting.

Dr. Wesley J. English then presented the communication from Community Health Services regarding a multiphasic screening program in Freeport and Pownal. Many questions relative to the funding and handling of patients in this program were raised. It was felt that this program be tabled until more information concerning its functions was available.

Resolutions on the deaths of Drs. Leon Babalian, David Davidson, and Horace K. Sowles were read respectively by Drs. Donald P. Cole, Walter B. Goldfarb and George L. Maltby. These resolutions will be spread upon our records and forwarded to the families. In addition, it will be sent to both the Maine Medical Center and Mercy Hospital staffs.

The next meeting was announced by Dr. Sylvester. It will be held November 21 at the Red Coach Grill in Portland. The program will be a general discussion of medical ethics as it applies to daily practice. The panel will be chaired by Dr. Robert E. McAfee.

The business meeting was adjourned by Dr. Sylvester at 9:30 p.m. Dr. Richard T. Chamberlin, Chairman of the State Professional Services Review Organization, then brought us up to date on the functions of his committee and the Pine Tree Organization. Following a lengthy question and discussion period, the meeting ended at 10:45 p.m.

ALFRED E. SWETT, M.D., *Secretary*

WASHINGTON

The regular meeting of the Washington County Medical Society was held on October 28, 1974 at the home of Dr. A. Cowan Collins, Dennysville, Maine, with 7 members and 7 guests present.

I. *Reading of Minutes:* Minutes of the previous meeting were not read, due to the fact a copy was not available.

II. *New Business:*

a. Applications for admission to the Washington County Medical Society were reviewed on an individual basis by the members present. Five applications were reviewed, individually voted on, and the following persons accepted into membership: Drs. Mark E. Battista, Patrick T. Minihan, Peter K. Hui, Carl K. Aselton, Jr. and John F. Murtaugh.

b. A delegate, Dr. Robert G. MacBride and an alternate delegate, Dr. Donald M. Robertson were elected to the House of Delegates of the Maine Medical Association.

At this point, we proceeded to the program. Mrs. Donna Allen, R.N., presented a description of Public Health Nursing Services within Washington County; the structure of her organization and the types of responsibilities the Public Health Nurses try to tackle.

Barry Kornrich presented the structure of Down East Health Services, showing the relationships of Maternal and Infant Care and Family Planning through Down East Health Services.

Michael Gougler then presented the concepts and philosophy of the Washington County Health Plan as a prepaid medical care program. Charles Scharenberg then presented the function of the Northeast Regional Health Council and described its functions.

Debate, discussion and even some clarification occurred during these presentations. It was generally agreed that this type of discussion represents a beginning effort to comprehend and perhaps coordinate the multiplicity of health system improvement efforts occurring in Washington County. It was agreed that at this time the concept of a professional assistant to the Secret-

ary of the County Medical Society could be of enough potential benefit to patient care, health delivery and the County Medical Society to warrant further investigation. It was resolved that a committee be formed to investigate the nature of this position, the qualifications of the person who would hold the position, design a variety of ways in which they could function and explore possibilities for financing the salary for such a position. Dr. Collins was appointed to that committee, a second member to be selected by Dr. Collins at a later date.

No further business or correspondence was brought up and the meeting was adjourned.

A. COWAN COLLINS, M.D., *Secretary protem*

LINCOLN-SAGADAHOC

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset, Maine on November 19, 1974.

The meeting was called to order at 8:30 p.m. by the President, Dr. Peter A. Evans. The minutes of the October meeting were read and accepted as written.

Old Business: Suggestions for nominating committee were asked for. Two names were forwarded and sent to M.M.A.

New Business: Dues for 1975. After a discussion of meal charges, the motion was made and seconded that 1975 dues be set at \$35; this amount was adopted by majority vote.

Dr. Evans then introduced Jerry Merrill and Ralph Osgood of Blue Cross and Blue Shield, who spoke of Blue Shield plans and fee schedules. A great deal of discussion of Usual, Customary, and Reasonable fee schedules and of income ceiling for service benefits took place.

Dr. Charles E. Burden moved that this Society request that Blue Shield stop offering 80 percent UCR on January 1, 1975 and that if that step is not taken, this Society agrees that all physicians in the Society will withdraw from participation in Blue Shield. Dr. David W. Schall seconded the motion. After discussion, the motion was withdrawn. Dr. Burden then moved that Blue Shield

be asked to drop the 80 percent UCR program on January 1, 1975 and encourage other county societies to reconsider their approval of this program. The motion was seconded with ten in favor and seven opposed.

The problem is Blue Cross funds paying for laboratory procedures in hospitals which Blue Shield funds will not cover in a doctor's office.

GEORGE W. BOSTWICK, M.D., *Secretary*

KENNEBEC

The November 21st meeting of the Kennebec County Medical Association was held at the Silent Woman Restaurant in Waterville, Maine. Following cocktails and dinner, the President, Dr. William E. Schumacher, called the meeting to order. The minutes of the previous meeting were accepted as read.

A letter from Dr. Charles E. Burden was read expressing concern about the Blue Shield UCR coverage program. After considerable discussion, Dr. Joseph J. Hiebel made a motion that the Association go on record as expressing our total opposition to the UCR plan with the 80 percent coverage feature, and directed that this sentiment be sent to the President of the Maine Medical Association and the Insurance Committee of the Maine Medical Association, with the request that the contract be rescinded. This motion was passed with one dissenting vote.

Two new members were elected. They were Dr. Sung Cho of Gardiner and Dr. James Butler of Waterville.

Dr. Schumacher then appointed a Nominating Committee consisting of Drs. George I. Gould, Chairman; Earl M. Davis and Brinton T. Darlington to present a slate of officers at the next meeting.

The speaker of the evening, Dr. John Serrage then outlined the recently established Regional Neo-Natal Intensive Care Program based at the Maine Medical Center in Portland. His presentation was well received and elicited considerable discussion.

The meeting was adjourned at 9:45 p.m.

KEVIN HILL, M.D., *Secretary*

NEWS FROM BLUE CROSS AND BLUE SHIELD — *Continued from Page 65*

illness. They indicate that the person is struggling actively with a situation that temporarily is beyond his capacity to master — inevitably so because of its nature or novelty."

Gerald Caplan, M.D.

Article: "Breakdown!? What To Do."

"People cherish the myth of themselves as restless, aggressive and pioneering; words like 'tranquility,' 'serenity' and 'calm' are rare in our vocabulary, in our schooling and in our lives. For most

of us, this means that we have paid an unconscious price that we generally start to feel in middle age — and which we accept as the dues of growing older."

Gay Luce and Erik Peper

Article: "Learning How To Relax."

"Stress" is available through the Communications Department, Maine Blue Cross and Blue Shield, 110 Free Street, Portland, Maine 04101.

Spring Meeting of the M.M.A. House of Delegates

Saturday, April 12, 1975

Thayer Hospital, Waterville, Maine

12:30 P.M. — Registration; 1:00 P.M. — Lunch; 2:00 P.M. — Meeting

10:00 A.M. — Meeting of the Executive Committee



The Journal of the Maine Medical Association

Volume Sixty-six

Brunswick, Maine, March 1975

Number 3

Clinical Applications of Multistage Exercise Testing

ROBERT F. KRAUNZ, M.D., F.A.C.C.*

Multistage electrocardiographic exercise testing provides a safe, non-invasive, and repeatable measure of cardiovascular performance. Many patients with heart disease will not manifest electrocardiographic abnormalities in the resting state. Approximately 70% of cases of angina pectoris without prior myocardial infarction will have a normal resting electrocardiogram.¹ Pathophysiologic abnormalities of diagnostic and prognostic importance, even when absent during the resting state, may be demonstrated during effort.

Since 1971, a variable speed-and-grade treadmill has been used to perform approximately 500 submaximal or maximal exercise tests at CMG Hospital. In the evaluation of patients with and without cardiovascular disease, we have found that multistage exercise testing has a wide clinical applicability. The treadmill has offered definite advantages over the Master's two-step test,² which we no longer use for routine exercise stress testing. The treadmill test involuntarily controls the rate of energy expenditure,³ permits continuous electrocardiographic surveillance during exercise for greater safety and diagnostic yield, and allows the attainment of a steady state at each incremental work level.^{4,5} The treadmill test imposes a greater work load than the two-step test and offers greater sensitivity in detecting overt or latent ischemic heart disease.^{4,8} Finally, treadmill exercise studies provide a basis for quantitative evaluation of functional capacity.^{4,6,9-11}

The following case reports illustrate the primary clinical applications of multistage treadmill tests employed at this hospital over the past three years.

*From the Department of Cardiology, Central Maine General Hospital, Lewiston, Maine 04240.

TABLE I

MULTISTAGE EXERCISE TEST				
Stage	Speed (mph) and % Grade	Minutes	Oxygen Costs ml/kg/min	METS
I	1.7 10%	1	11.2	3
		2	14.2	4
		3	17.2	5
II	2.5 12%	4	20.1	6
		5	23.0	6.5
		6	26.0	7
III	3.4 14%	7	29.0	8
		8	31.9	9
		9	34.8	10
IV	4.2 16%	10	37.7	11
		11	40.7	12
		12	43.6	12
V	5.0 18%	13	46.5	13
		14	49.5	14
		15	52.4	15

Methods

We use a continuous multistage treadmill test according to the Bruce protocol.^{4,7} Exercise is divided into several stages, each of three minutes duration, beginning at a low level of 1.7 mph and a 10% grade (Table I). On occasion, it is necessary to begin patients with very poor exercise tolerance at a lower speed and incline. After signing an informed consent form, the patient is asked to walk continuously on the treadmill through successive stages until fatigue, dyspnea, or other symptoms necessitate stopping. A maximal or near maximal effort is strongly encouraged. Continuous oscilloscopic monitoring is performed during the procedure, and a physician is in attendance. Full resuscitative equip-

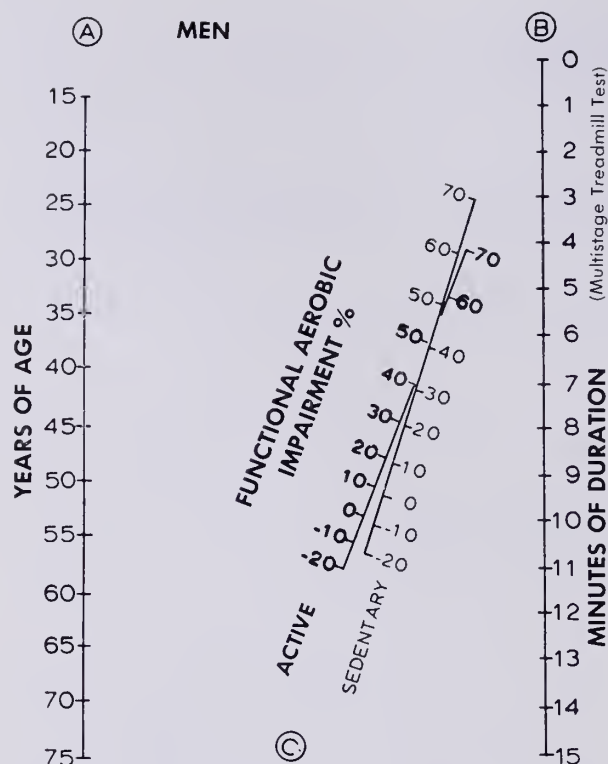


Fig. 1. Nomogram to assess FAI in men according to age, duration of exercise, and habitual physical activity status. Reproduced with permission from RA Bruce.¹⁰

ment, including a D-C defibrillator, is available but has never been required. The test is discontinued by the physician when conduction disorders, serious rhythm disturbances, or pronounced ST segment depression occur.

A 12 lead resting electrocardiogram (ECG) is obtained prior to the exercise test. A transthoracic bipolar lead from the inferior tip of the right scapula to the V5 position with a ground electrode over the right clavicle is used to monitor the electrocardiogram for rhythm, rate, and ST-T wave changes during and following exercise. An ECG strip is taken as a control at rest, during each stage of the test, immediately following exercise (0 recovery), and at 1½, 3, 5, and 8 minutes following exercise. Blood pressure is measured at rest and at 0, 3, and 8 minutes recovery. The ECG strips obtained during and following exercise are examined for ST segment changes and rhythm disorders. A definitely positive response is defined as a 1 mm. (0.1 mv) or more horizontal or downsloping depression of the ST segment during or after exercise. Junctional depression with an upsloping contour of the ST segment and return to the isoelectric reference line (PQ segment) within 0.08 seconds after the J point is considered normal. If the ST segments are upsloping with 1 or more mm. of depression 0.08 seconds beyond the J point, then the test is considered equivocal or suggestive

of ischemia, depending on the degree of depression.^{4,12-14}

A close relationship exists between the total duration of exercise and the amount of oxygen consumed, and maximal exercise correlates with maximal oxygen consumption ($\dot{V}O_2$ max). Adjustment of $\dot{V}O_2$ max for age, sex, and activity allows for comparison of a given patient with his peers by use of the term, functional aerobic impairment (FAI).^{9,10} This parameter can be expressed as follows:

$$FAI = \frac{\text{Predicted } \dot{V}O_2 \text{ max} - \text{observed } \dot{V}O_2 \text{ max}}{\text{Predicted } \dot{V}O_2 \text{ max}} \times 100$$

A relative measure of functional aerobic capacity would equal 100% - FAI. It is not feasible to measure actual oxygen consumption during clinical exercise testing. Since the total duration of maximal exercise correlates closely with maximal oxygen consumption, normal standards and test results can be compared by nomograms, illustrated in Figure 1. Separate nomograms for men and for women have been compiled from data in normal subjects of different sex, age, and habitual physical activity.^{9,10} A straight edge intersecting age (in years) and total duration of exercise (minutes) provides an immediate value for FAI. The severity of impairment is rated as follows:

Impairment	FAI
None	-20 to +23%
Minimal	24 to 35%
Moderate	36 to 47%
Marked	48 to 59%
Extreme	59% or more

Average oxygen requirements are expressed in ml O_2 /kg/min in Table 1. The values for normal women are similar and are not included here. Work intensity can also be expressed as METS, representing multiples of the basal metabolic rate (Table 1).

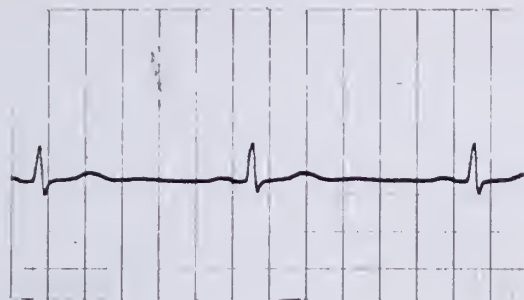
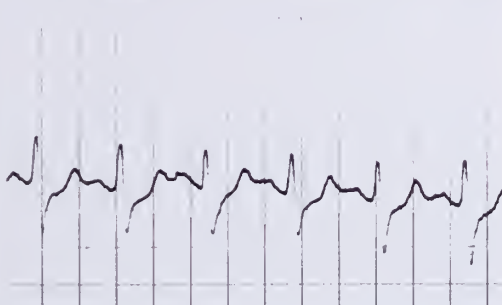
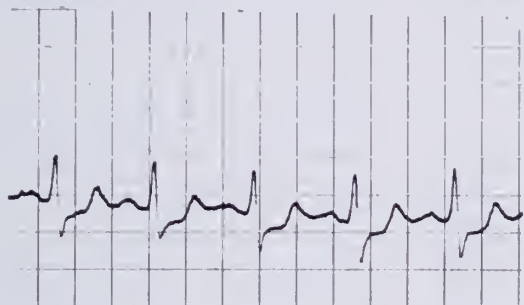
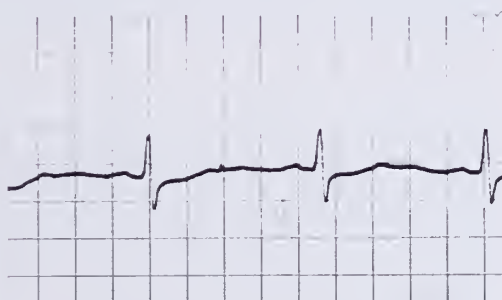
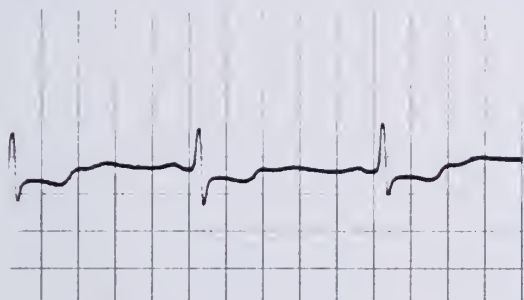
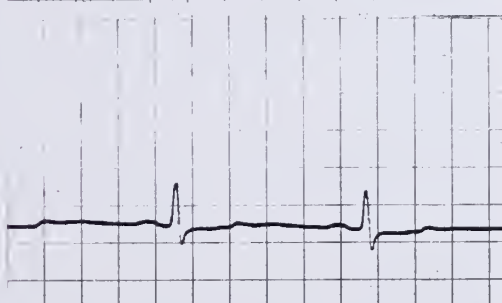
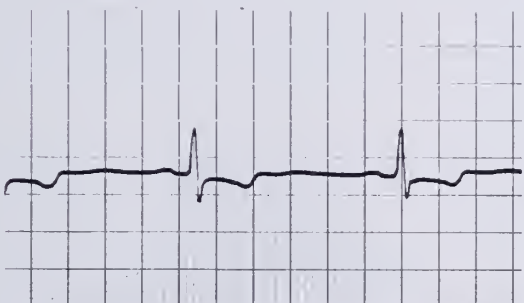
Case Reports

Case 1 - A 55-year-old dairy farmer was admitted to the CMG in September 1974 because of two episodes of pain involving his left arm, left shoulder, and anterior chest. Each episode lasted 45 minutes. Serial electrocardiograms demonstrated ST coving and T wave inversion in leads I, L, and V2 thru V5, suggesting anterolateral intramural infarction. The initial SGOT was slightly increased to 28 units (normal < 12 units). Otherwise, the enzyme tests, including SGOT, CPK, and LDH, were normal for three days. A lipoprotein electrophoresis showed a Type IV pattern. His hospital course was uneventful, and he was discharged on prophylactic propranolol and nitroglycerin (NTG) as needed. On 10/22/74, a resting electrocardiogram was normal without the previous repolarization changes. A multistage treadmill test was performed, and he stopped after 7½ minutes in Stage III because of discomfort in his left elbow and left shoulder. The maximal heart rate (HR) was 115, and there was 2 mm of ischemic ST segment depression immediately after exercise (Fig 2a). Downsloping ST depression persisted until 8 minutes after exercise. Fol-

FIRST EFFORT

AFTER NTG

CONTROL

0
RECOVERY3 MIN.
RECOVERY5 MIN.
RECOVERY

(a)

(b)

Fig. 2. Case 1. (a) Exercise-induced ischemic ST segment changes persisting during the recovery period. Maximal heart rate 115. (b) Repeat test following nitroglycerin. Junctional changes at 0 recovery with heart rate 132, and return of ECG to normal by 3 min. recovery.

lowing nitroglycerin, the patient was asymptomatic after three complete stages, and the HR rose to 132. The ECG showed equivocal changes with 1½ mm. of junctional depression and up-sloping ST segments at 0 recovery with return to control appearance by 3 minutes recovery (Fig 2b.). Over the next few weeks, he continued to have exertional chest and shoulder discomfort. Cardiac catheterization and coronary arteriography at the Maine Medical Center in early December showed an 80% obstruction of the left anterior descending artery. Left ventricular function was adequate, and the patient successfully underwent coronary artery bypass surgery in January 1975.

Comment: This case illustrates how exercise electrocardiography can be used to confirm the clinical diagnosis of coronary artery disease and to estimate the severity of the disease process. The strongly positive treadmill test demonstrated significant myocardial ischemia during exercise, which corroborated the clinical suspicion of a high-grade, proximal obstruction in a major branch of the left coronary artery. A critical lesion was subsequently

demonstrated by coronary arteriography. Davia et al observed that 73% of 37 patients with 2 mm. or more ischemic ST depression on treadmill tests had critical lesions demonstrated by arteriography in the main left coronary artery or its major branches.¹⁵ In this patient, a treadmill study was also useful in evaluating the response to nitroglycerin (Fig. 2), which provided both subjective and objective improvement. The treadmill test is easily repeated and permits ready analysis of short or long-term treatment.

Case 2 – This 51-year-old man was a healthy construction worker until June 1972 when he was admitted to another hospital with a well-documented acute, inferolateral myocardial infarction. His hospital course was uncomplicated, but the recuperative period was characterized by atypical, squeezing pains over the cardiac apex unrelated to exertion and not promptly relieved by nitroglycerin. He had a history of chronic anxiety. He was sent to me for disability determination. Physical examination showed a tense man, with cold, moist hands. The cardiovascular examination was unremarkable. In November 1972, a resting ECG showed sinus tachycardia and a stable inferior wall myocardial infarction. He walked 1 minute into Stage IV on the treadmill for a total of 10 minutes. He stopped with dyspnea and a slight pain in his left anterior chest. The FAI was 5%, normal for active men his age. His maximal heart rate was 170, and ischemic ST changes did not occur.

Comment: Patients recovering from myocardial infarction should undergo an objective evaluation of physical capability.^{4,6} The response to an effort test a few months after infarction is useful in the rehabilitative process, and it provides necessary information for advising patients about occupational activities, recreation, and physical conditioning programs.^{5,6,16}

Atypical chest pain syndromes occur frequently after a myocardial infarction and are often difficult to evaluate. A completely negative exercise test suggests that the chest discomfort may be unrelated to coronary heart disease. Exercise tests are particularly sensitive indicators of left anterior coronary artery disease,¹⁷ so a negative test in a patient with a prior inferior wall infarction may be especially informative.

Case 3 – This 53-year-old housewife had a proven inferior wall myocardial infarction in June 1968. There was a prior eight-year history of hypertension, moderately well controlled with diuretics. In 1971, she began to have effort-related chest pain, sometimes characteristic of angina pectoris. In addition, she had frequent atypical chest pains with a burning quality encircling her left chest, persisting for several hours, and inconsistently relieved by nitroglycerin. Her symptoms were thought to be partially related to a chronic anxiety — depressive reaction.

Several cardiovascular examinations revealed blood pressures in the 160/90 range, a left ventricular thrust 12 cm from the midsternal line, a Grade I systolic ejection murmur at the mid-left sternal border, and a soft apical S4 filling sound.

In May 1973, propranolol resulted in marginal improvement of her anginal syndrome. A treadmill test was performed in July 1973 (Fig 3a). The resting ECG showed an old inferior wall infarction and left ventricular hypertrophy. She was able to tolerate 3½ minutes of the test and stopped in Stage II with anterior

chest pain radiating to the posterior cervical area. The FAI was 50% indicating marked impairment. The test was strongly positive with 6 mm of ST depression at 0 recovery. T wave inversion was noted, and the ST segment abnormality persisted for 8 minutes following exercise. In December 1973, she was hospitalized with an anterolateral subendocardial infarction. The serum enzymes were minimally elevated. After several pain episodes following discharge, she finally agreed to coronary arteriography, performed at the Maine Medical Center in March 1974. This procedure showed significant three-vessel coronary artery disease with an 80% obstruction of the left anterior descending branch, occlusion of the right coronary artery, and moderate obstructive changes in a small circumflex branch.

In April 1974, the patient underwent saphenous vein bypass grafting to the left anterior descending and right coronary arteries. There was dramatic improvement following surgery with full resolution of her anginal syndrome. The exercise test was repeated in October 1974 (Fig 3b). The control tracing showed 2 mm of ST depression which increased to 4 mm during Stage II and at 0 recovery. By 5 minutes post-exercise, there was a return to the control tracing. The patient was able to walk into Stage III for a total of 6½ minutes. FAI was 15%. Compared to active, normal women her age, functional capacity was normal. At the time of the second treadmill, the patient had been taking digoxin for several months.

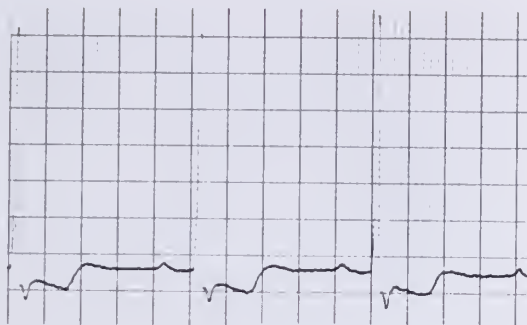
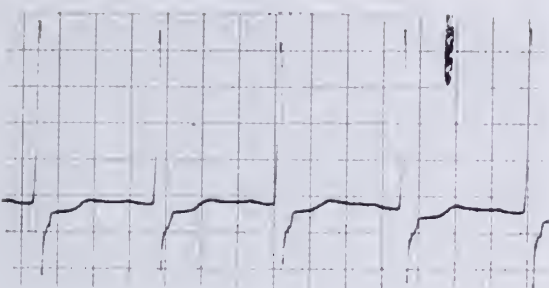
Comment: The initial treadmill test was helpful in providing objective evidence of ischemic heart disease in this chronically depressed and anxious woman with a low pain threshold and several somatic complaints. Her effort-related angina pectoris was not controlled by adequate doses of propranolol, leading to coronary arteriography and a double saphenous vein bypass procedure. The postoperative ECG stress test documented some improvement in the magnitude and persistence of post-exercise ST segment depression even though she was on digoxin at that time.¹⁸ Her overall exercise tolerance was also greatly improved. This again illustrates the usefulness of stress testing in evaluating the effectiveness of a therapeutic procedure, in this case aortocoronary bypass surgery.

Case 4 – The patient is a 39-year-old electronics technician known to have a heart murmur since age 16. In October 1972, he was admitted to the CMG Hospital for hemoptysis. At that time, he claimed that he had always been active without exertional dyspnea, and he denied other cardiovascular symptoms except for episodic palpitations. The physical examination was compatible with classical mitral stenosis. At the cardiac apex, there was a Grade III presystolic murmur and a prolonged Grade IV diastolic rumble. There was a sharp opening snap best heard at the low left sternal border. An electrocardiogram showed "P-mitral" indicative of left atrial enlargement. The chest x-ray revealed Kerley B lines in the lower lung fields and a double cardiac contour consistent with left atrial enlargement. An echocardiogram was compatible with tight mitral stenosis. An exercise test was performed to obtain a more objective assessment of his functional capacity. He was able to walk a total of only 4 minutes, indicative of marked aerobic impairment (FAI = 58%). He had frequent short runs of paroxysmal atrial tachycardia during Stage II and at 0 recovery, but no ischemic ST segment changes were noted. A right and left heart catheterization at the CMG confirmed the diagnosis of significant mitral stenosis with a mean pulmonary artery pressure of 54 mm Hg and a pulmonary wedge pressure of 32 mm Hg. No mitral regurgitation was evident by left ventriculography. In February 1973, a closed mitral valvulotomy was performed at the Maine Medical

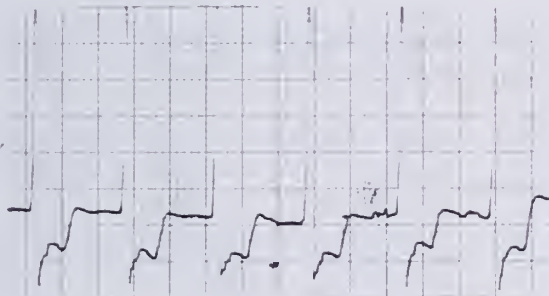
7/73
PRE-OP

10/74
POST-OP

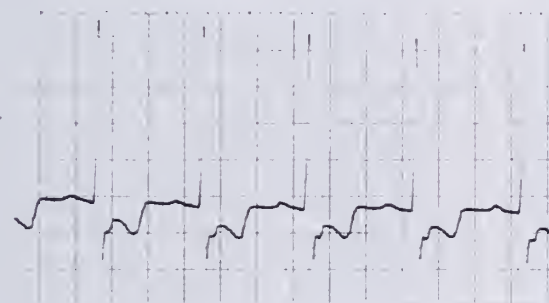
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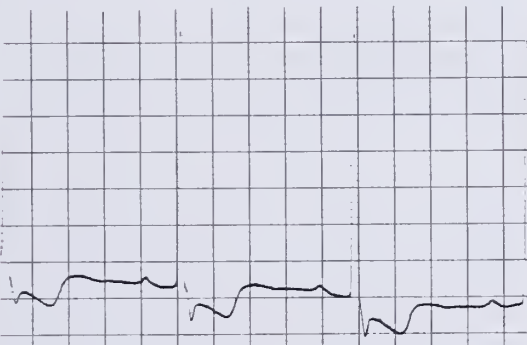
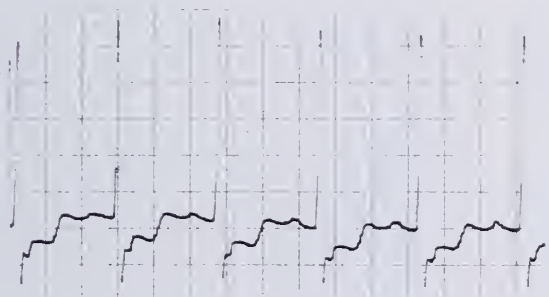
0
RECOVERY



3 MIN.
RECOVERY



5 MIN.
RECOVERY



(a)

(b)

Fig. 3. Case 3. (a) Prior to coronary bypass surgery the exercise response was strongly positive. (b) Following surgery a repeat test was positive with return to control ECG 5 min. post-exercise.

Center without difficulty. The tightly stenotic valve was opened to better than two fingerbreadths with transventricular dilatation. By May 1973, he was able to assume full activities and he commented that he had not realized how limited he had been prior to

surgery. A repeat exercise test was performed in September 1973 and he was able to continue into Stage IV for a total of 9½ minutes. The FAI was 22%, a considerable improvement from his preoperative study. No arrhythmias or ST segment changes

were observed.

Case 5 – This 65-year-old school teacher was found to have a heart murmur at age 35. She had intermittent palpitations for several years, culminating in chronic atrial fibrillation in 1966. The ventricular rate was controlled with 0.1 mg of digitoxin daily. For several years, she felt well and was able to continue her daily work as a school teacher and housewife. She was aware of some dyspnea on climbing one flight of stairs rapidly. Initial evaluation in March 1971 showed atrial fibrillation with a controlled ventricular response of ± 80 . There was no evidence of right ventricular hypertrophy. The first heart sound was accentuated at the apex. There was a definite opening snap heard along the left sternal border, and a diastolic rumble was present at the apex. The ECG showed an R/S ratio of 1 in V1, suggesting right ventricular hypertrophy. A chest x-ray revealed left atrial enlargement with posterior displacement of the barium-filled esophagus. There was no central pulmonary congestion or redistribution of blood flow to the upper lung fields. An echocardiogram demonstrated the characteristic pattern of moderate mitral stenosis. In October 1972, the patient claimed that walking 10 to 12 steps necessitated stopping with some shortness of breath and cardiac "pounding." At that time, an exercise test was performed for more objective functional evaluation. She was able to continue into Stage III for a total of 8 minutes. This represented an FAI of $\sim 20\%$, an excellent performance. The exercise-limiting symptom was fatigue, not dyspnea, despite a maximal heart rate of ± 200 . Because of her normal exercise tolerance, a cardiac catheterization was not performed. In the past two years, her minimal symptoms have not progressed, and there have been no objective changes in her status by physical examination, ECG, or chest x-ray.

Comment: These two cases exemplify the use of a standardized maximal exercise test in assessing the functional capacity of patients with valvular heart disease. Impairment may be more objectively evaluated by this method than by the clinical history.¹⁹ In Case 4 the treadmill test demonstrated severe exercise intolerance in a stoic man with tight mitral stenosis who had not been aware of his cardiovascular limitation. In Case 5, effort testing demonstrated good exercise tolerance in an elderly woman with long-standing mitral stenosis. Patients with valvular heart disease can be serially tested, and a worsening functional capacity may indicate a need for surgical correction.⁵ However, we do not perform multistage treadmill tests on patients with hemodynamically significant aortic stenosis.

Case 6 – This 58-year-old man began to have dizzy spells with transient blurring of vision and momentary loss of balance in March 1973. In September of that year, he noted intermittent substernal pressure lasting approximately one minute and unrelated to exertion. On 11/13/73, he was hospitalized for evaluation of a syncopal episode with loss of consciousness for fifteen minutes, during which time he was incontinent of urine and completely unresponsive to verbal stimuli. The cardiovascular examination was unremarkable except for a sinus bradycardia of 48 beats/min. Cardiac monitoring revealed a persistent sinus bradycardia with a brief episode of ventricular bigeminy associated with a transient bundle branch block. Slight peaking of the precordial T waves was seen on the resting ECG. A treadmill test was then performed. During Stage III, the patient stopped with slight dizziness and dyspnea, and short runs of ventricular tachycardia were observed at 0 recovery. (Fig 4). The maximal sinus rate was 128. The ST segments were upsloping with 1 mm depression 0.08 seconds after the J point. At five minutes post-

exercise, these changes had resolved. Therapy with quinidine sulfate was initiated, and the patient was discharged on that drug. On 11/19/74, he suddenly collapsed and required cardiopulmonary resuscitation. After a brief hospital stay at the CMG and a change in his drug program to procainamide, he was transferred to the Maine Medical Center for coronary arteriography. Prior to this procedure, an episode of ventricular fibrillation was observed by telemetry, and prompt electrical defibrillation was performed. On one occasion, he had chest discomfort associated with transient ST segment elevation. Coronary arteriography was normal except for a 50% obstruction in the proximal mid-third of the right coronary artery. The injection was routinely performed following nitroglycerin. When the catheter was placed into the left ventricle, spontaneous ST elevation and QRS prolongation were observed. These changes resolved after sublingual nitroglycerin and withdrawal of the catheter into the ascending aorta. The left ventriculogram demonstrated a short akinetic segment along the inferior wall and a slightly low ejection fraction of 62%. A diagnosis of Prinzmetal's syndrome was made.²⁰ It was thought that spasm at the site of partial right coronary artery obstruction produced significant myocardial ischemia and ventricular irritability. Consequently, the patient underwent an uneventful right aortocoronary artery bypass graft on 12/3/73. A follow-up catheterization in late February 1974 showed a fully patent bypass graft. Following surgery, the patient became asymptomatic and returned to work in June 1974. The paroxysmal ventricular irritability has not recurred.

Comment: This man presented with a major syncope episode preceded by a six-month history of dizzy spells. Initially, a bradyarrhythmia was thought to be the cause of his symptoms. Exercise stress testing demonstrated that ventricular irritability was, in fact, the major problem. A strikingly similar case was recently described.²¹ The patient was a 47-year-old man with syncope, periodic ST segment evaluation, and recurrent ventricular tachyarrhythmia associated with obstruction of the right coronary artery. Bryson and colleagues²² reported three patients with clinical ischemic heart disease who developed ventricular tachycardia during a standard exercise test. Although apparently adequate drug therapy was instituted, subsequent exercise testing demonstrated recurrent ventricular tachyarrhythmias at modest work levels. In each case, successful saphenous vein bypass graft surgery was performed, and the arrhythmias were terminated. Several other reports have reviewed the usefulness of exercise testing in eliciting significant arrhythmias.²³⁻²⁷ Kosowski et al showed that treadmill exercise testing yielded a higher incidence of ventricular premature beats and more than twice as many major ventricular arrhythmias as prolonged ambulatory ECG (Holter) monitoring.²⁶ In patients with known coronary artery disease, the induction of ventricular arrhythmias by exercise testing bears a close relationship to the extent of vessel involvement and to the occurrence of ventricular contractile abnormalities.²⁵ Detecting major ventricular rhythm disorders during effort may serve to identify patients who are at a higher risk for sudden death.^{24,27}

Discussion

The multistage exercise stress testing has several

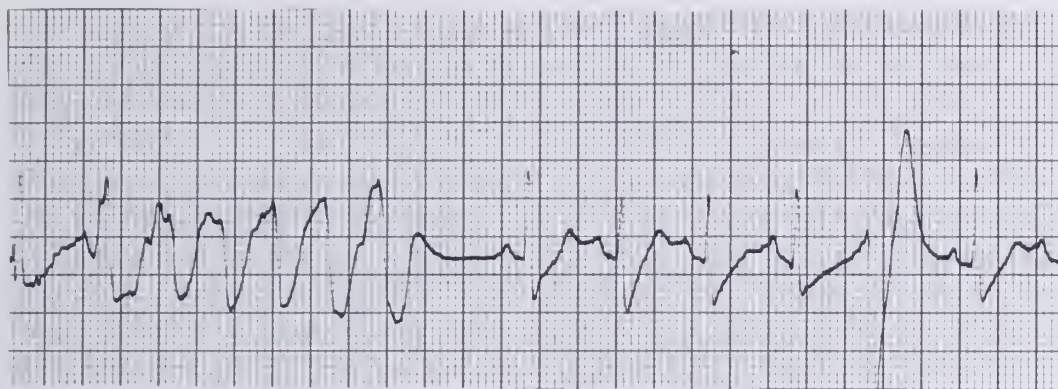


Fig. 4. Case 6. A 58-year-old man with single vessel coronary artery disease. Ventricular irritability present at 0 recovery.

broad clinical applications which have been categorized⁵ as follows:

Diagnosis: The detection of exertional myocardial ischemia may clarify the differential diagnosis of a chest pain syndrome.^{4,6} In some reports, the ischemic ST segment response has correlated with location and extent of coronary artery disease.^{13,15,17,28} In our general experience, the patients whose treadmill studies have shown more than 2 mm of ST segment depression, particularly at low levels of exercise, have had high-grade, proximal lesions in the coronary circulation and have usually required coronary artery bypass surgery. Cases 1 and 3 are representative of this group.

For proper interpretation, the clinician must be aware of inherent limitations of graded exercise testing in the diagnosis of ischemic heart disease. An appreciable number of false positive and false negative tests occur.^{5,6,13,14,28} One could argue with the use of these terms because they are based on coronary arteriography as a standard of comparison. While arteriography affords visualization of the coronary arterial circulation, it does not reveal the balance between myocardial perfusion requirement and supply. Exercise tests, on the other hand, may demonstrate insufficient myocardial perfusion during stress but do not provide anatomic information. The two tests are thus complementary, effort testing supplying indirect physiologic data, and arteriography localizing anatomic obstructions.

In several reports,^{13,28,31} the sensitivity of graded exercise testing based on coronary arteriography has ranged between 62% and 82%. The occurrence of a patient's typical chest pain during the test^{5,30,31} and the discontinuation of drug therapy prior to testing^{13,28} appear to enhance sensitivity. Patients with a false negative response are likely to have their coronary disease limited to a single artery, usually the right coronary or left circumflex, and the sensi-

tivity of exercise testing is greater in patients with two or three vessel disease.^{13,15,17,28} Bruce believes that relying on ST segment changes alone for interpretation may be misleading and that the exercise test should be considered an important extension of the clinical examination.³² Pertinent observations can be made during and following the tests, and information regarding motivation, attitude, and the relationship between subjective symptoms and objective signs can be obtained.

As shown in Case 6, a treadmill study may be extremely useful in the detection of an effort-related rhythm disorder (Fig. 4). This serves in the evaluation of symptoms such as palpitations, dizziness, or syncope; and the observation of an arrhythmia or conduction abnormality during an exercise test may identify the cause of the presenting complaint.

Positive exercise tests occur in approximately 5 to 15% of patients with normal coronary arteriograms (false positive).^{13,28,31} Such a response might occur from relative coronary insufficiency due to ventricular hypertrophy or anemia. Other causes of false positive exercise tests include digitalis,¹⁸ hypokalemia, rheumatic heart disease, and cardiomyopathy.⁵ Similarly hyperventilation,³³ vasoregulatory abnormalities,³⁴ and sedative or cardiovascular drug therapy^{13,28} may cause ST segment changes in the absence of coronary artery disease.

Prognosis: Several studies have demonstrated the value of submaximal exercise testing in predicting the future manifestations of ischemic heart disease.³⁵⁻³⁹ Doyle and Kinch showed a thirty-fold increase in the risk of developing clinical coronary heart disease within five years after a positive exercise response.³⁷ Blackburn and his associated observed that a positive exercise test has a prognostic significance independent of other risk factors.³⁹ More recent investigation suggests that maximal effort testing may be even more sensitive as a

screening tool for latent coronary artery disease.⁴⁰ The epidemiologic implications for broad population studies are apparent. On a clinical level, maximal treadmill responses could be used to screen patients in particularly dangerous occupations or those vulnerable to the development of coronary heart disease because of other prominent risk factors.

Functional Assessment: The maximal exercise test provides a quantitative assessment of aerobic capacity, an accepted standard of physical fitness. The measurement of a patient's performance capacity by treadmill testing permits a more objective evaluation of cardiovascular impairment than the clinical estimation of functional class.¹⁹ We have found nomographic measurements of FAI^{9,10} (Fig. 1) particularly useful for this purpose. Exercise tests can be used to assess the functional capacity of patients with all types of heart disease, including ischemic,^{4,6} valvular,⁵ and congenital.⁴¹ Exercise studies also allow serial evaluation of patients with heart disease and thus provide valuable data for therapeutic decisions.

The evaluation of physical performance capacity provides a sound basis for recommendations on occupational and recreational activity,⁶ even in patients who are recovering from a recent myocardial infarction. The treadmill test is helpful in formulating an exercise prescription for patients with or without heart disease, and a vigorous study may increase individual motivation for entering and adhering to an exercise program.³

Effects of Drugs and Specific Therapeutic Programs: Multistage exercise electrocardiography provides a repeatable and non-invasive procedure for evaluating the effect of a number of therapeutic interventions. This includes drugs such as propranolol, nitroglycerin (Fig. 2), or antiarrhythmic agents; rehabilitative methods including physical training; and aortocoronary bypass grafting (Fig. 3) and other surgical procedures.

Summary

Six cases have been reported illustrating important clinical applications of exercise stress testing. A multistage treadmill test for exercise electrocardiography provides significant diagnostic and prognostic data in the evaluation of patients with coronary artery disease. It permits quantitative assessment of functional capacity in all types of patients with or without cardiovascular disease. Finally, exercise studies are safe and easily repeatable for evaluating the effect of various therapeutic interventions. The clinician must be aware of the imperfect association between exercise testing and coronary arteriography and the numerous clinical con-

ditions which may interfere with the proper interpretation of the exercise response.

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Renal Failure in the Small Center: The Long and the Short of It

FRANCIS X. FELLERS, M.D.*

About 2% of a general hospital's admissions will represent diagnoses of concern to a Nephrologist. The greater majority of these diagnoses however will not require his expertise. When the patient with renal failure presents himself, can his care be managed adequately to allow a safe referral to the larger center for definitive care?

In the course of a year, two (2) patients were admitted to Central Maine General Hospital with severe renal failure.

Case 1. A 15-year-old youth in late spring, ingested approximately 40 ml. of Prestone® antifreeze following a family quarrel. A few minutes later, he told his parents, and they rushed him to the Emergency Room. After obtaining a chest x-ray which was unremarkable, he was sent home. About 8 hours later he had difficulty walking, and when brought to the Emergency Room, was admitted. During the night, he vomited several times. Next morning, he was sleepy, disoriented. The laboratory data showed severe metabolic acidosis with serum bicarbonate 2 mEq/L, pH 7.11, and potassium 7.2 mEq/L. Oliguria and anuria rapidly developed. He was promptly transferred to the Maine Medical Center. Following several days of dialysis, urinary output increased. Recovery then ensued rapidly and he was returned to a physician's care in his community. Other than polyuria of several months' duration, he has remained well with negative urinary sediment.

Case 2. A 56-year-old male truck driver was admitted to the Central Maine General Hospital for evaluation of acute onset of vomiting and "not feeling well." Thirty (30) years prior, he had been intensively evaluated elsewhere for protein in the urine, but no diagnosis given. For the past fifteen (15) years, he took a medication for high blood pressure. His pressure was adequately controlled since he was able to pass the yearly Interstate Commerce Commission physical exams for truck-drivers' licensure. He remained robust and healthy, a small meat-eater, but drank considerable amounts of fluids and always had to get up at night usually twice to urinate. His initial laboratory work showed severe renal failure, creatinine over 20 mg/100 ml, phosphorus over 12 mg/100 ml, derived bicarbonate 9 mEq/L, uric acid over 20 mg/100 ml, and hemoglobin 7 gm/100 ml. Intensive fluid and electrolyte therapy with 2 units of packed red cells over a 3-week period resulted in slow and progressive improvement. The blood data showed the creatinine down to 8 mg/100 ml., phosphorus 7 mg/100 ml and hemoglobin stabilized at 7.5 gm/100 ml. The patient was ambulatory and able to ingest his restricted diet with fluids of 2 to 3 liters daily and salt ad lib. Arrangements were made for referral for end-stage renal disease management.

Both patients had severe renal failure and survived, but neither was recognized as renal failure at the time of presentation at the hospital. The extremely uncommon occurrence of this life-threatening

condition would explain this lack of recognition. The rapid (patient blood profile) on a routine basis on sick patients would appear to meet this problem adequately and allow the recognition of the correct diagnosis.

In both patients, the diagnosis of impending renal failure should have been recognized. The abrupt hospitalizations could have been prevented. Acute renal failure in the young adult can be classified in three (3) general categories:

Acute Glomerulonephritis — post-streptococcal, necrotizing, anaphylactoid purpura, membranoproliferative and IGA types

Acute Tubular Necrosis — secondary to shock/hemorrhage/burn, toxic substance, drugs

Acute Obstructive — stone, bleeding, prostatism

Chronic renal failure can similarly be grouped:

Chronic Nephritides — glomerulonephritis, familial, Lupus, membranoproliferative, nephrotic

Chronic Pyelonephritis

Chronic Obstructive Disease

Congenital Anomalies — polycystic renal disease, nephronophthisis, medullary cystic

Vascular Disease — diabetes

The first patient presented within one (1) hour of ingestion of ethylene glycol, a known nephrotoxic agent. A prompt gastric lavage or successfully induced emesis could have removed the offending agent easily if carried out as indicated. If the delay time was significantly longer, the administration of 30 ml. ethyl alcohol orally or IV at 2-hourly intervals would metabolically interfere with the continuing oxidation of the glycol by alcoholic dehydrogenase and thus prevent the severe metabolic acidosis. The concurrent administration of fluids would permit urinary excretion of the glycol. At an even later delay time, the promotion of an osmotic diuresis with 300 ml. 15% mannitol at 2-hourly intervals with close observation of total fluids and electrolytes needs would prevent tubular necrosis. By admission, the 24-hour delay had already allowed the acute renal failure to develop completely.

In the second patient, the knowledge of protein in the urine thirty (30) years previously, followed by hypertension for the past fifteen (15) years, should require a continuous monitor of renal function with serum creatinines. Serum levels over 6 mg/100 ml indicate the need for referral to an end-stage renal disease center for definitive care in near future. In

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The Unusual Presentation of "Juvenile" Rheumatoid Arthritis in an Adult

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The workup of fever of unknown origin (FUO) can be one of the more challenging experiences in the realm of internal medicine. Various infections, vasculidities, tumors, and even inflammatory bowel disease can all present with the one sign of persistent or spiking fever. One of the more unusual causes of FUO is represented by the adult presentation of Still's disease, which when it presents in childhood, is marked by fever, joint symptoms, lymphadenopathy, and splenomegaly as opposed to primary joint involvement seen in classical rheumatoid arthritis. The following case is presented as an example of this unusual syndrome.

CASE PRESENTATION

The patient is a 30-year-old Gravida 3, Para 2, Abl Caucasian woman who presented in September 1972 with the chief complaint of flank "soreness" and daily temperature spikes. The patient was perfectly well until April 1972 when she noted a low-grade fever, especially in the evenings, one or two days out of each week. She did notice a confluent erythematous and macular rash on the medial aspect of her thighs and upper arms which would appear during her fevers and usually subside, although not completely so, after the temperature subsided. At one point, her temperature spiked as high as 104 degrees. In May 1972 she began having bilateral flank pain varying in intensity from side to side and was told that she might have a "kidney infection." After one course of antibiotics which had no effect, the patient was admitted for evaluation. At that time in July 1972, her temperature was 102 degrees and there was tenderness in the left flank without a palpable mass. Urinalysis revealed 15-20 WBC's and 5-10 RBC's with 1+ albumin. Hematocrit was 32%. An IVP revealed normal kidneys but there was a suggestion of splenic enlargement although no spleen was felt clinically. A Coomb's test was negative and a reticulocyte count was normal. Urinalysis did reveal *Streptococcus faecalis* and the patient was treated with Loridine® and discharged on Microdantin. Upon discharge, the symptoms recurred and she was readmitted to the hospital in August 1972. This time the pain was in the right flank and the temperature was 102 degrees. Urinalysis was normal and no definite diagnosis could be made. An antibiotic was discontinued when no definite organism was found. Upon further questioning, it was discovered that the patient admitted to having a faint macular, erythematous non-pruritic rash on the medial aspect of both arms and thighs for over a year which had been asymptomatic and essentially ignored.

Past medical history includes a cholecystectomy at the age of 20 for stones and several gynecological procedures seven years before which culminated in a hysterectomy and ovariectomy. The only medication that she had been taking was intermittent aspirin and Premarin® 1.25mg. cyclically. The patient had been exposed to no farm animals and had not been traveling out of the

country. Family history was remarkable in that her mother had classical rheumatoid arthritis for many years and a sister developed rheumatism at the age of 35.

Physical examination in September 1972 as an outpatient revealed no lymphadenopathy or splenomegaly. There was a macular erythematous rash on the medial aspects of both arms and thighs radiating around to the buttocks. There was no facial eruption of any kind. There was bilateral flank tenderness to percussion, left greater than right. The patient was readmitted to the hospital for the third time. There laboratory tests revealed a hematocrit of 32% with a slight leukopenia of 5,700 with normal differential. Platelets were 400,000 per cubic millimeter. Sedimentation rate prior to admission was 130 mm/hr. Skin test for TB, histoplasmosis, and coccidioidomycosis were negative with PPD carried out to second strength. Febrile agglutinins were negative. SMA/12 was normal. ANA and rheumatoid factors were negative, both as outpatient and inpatient. Stools were negative for ova and parasites. In the hospital, the patient was found to have a documented fever, usually spiking between 6 and 8 p.m. daily, averaging 103 to 105 degrees. There were no associated chills. Blood and urine cultures revealed no growth. LP revealed a slight pleocytosis with 4 polys and 2 lymphs but no growth. Spinal fluid glucose and protein were normal. The entire bowel series, including the small bowel follow through, was normal. Chest film revealed no hilar adenopathy and was normal. Biopsies of the quadriceps muscle and skin were normal. Biopsy of the area of rash revealed only minimal nonspecific infiltration of inflammatory cells, mostly polymorphs. Percutaneous liver biopsy (Klatskin) revealed only minimal pericholangitis and no granulomatous lesions were seen. A bone marrow revealed about 20% mature eosinophils but no other abnormalities.

The patient was begun empirically on Prednisone and discharged on 50mg. per day. On this dose, her temperature disappeared but she persisted in having moderate flank pain. Sedimentation rate fell to 8mm/hr. Her hematocrit increased to 42%. In spite of this initial improvement, the patient was readmitted to the hospital in October 1972 because of persistent flank pain. At this time, a laparotomy was performed. A spleen 3 times normal size was found which pathologically revealed only diffuse hyperplasia. No lymphadenopathy was found in the retroperitoneum. An operative liver biopsy was done which was normal. Needle biopsy of the kidney was carried out which appeared normal although no glomeruli were obtained. Lymph nodes taken at the time of surgery revealed only reactive hyperplasia. There was no evidence of malignancy. The month after splenectomy she was free of flank pain and Prednisone was decreased to 2.5mg. per day. On that dose, she developed what appeared to be erythema nodosum on the anterior tibia bilaterally. This disappeared on a transient increase in Prednisone and has not returned. The patient did not have sun sensitivity when she was carefully observed during the summer months. The patient enjoyed a nine month remission from symptoms until July of 1973 when she developed pain in the right knee and left hip associated with a fever of 102 degrees. It was at that time that a diagnosis of an adult form of juvenile rheumatoid arthritis was considered and the patient was started on high-dose aspirin (1200mg. q4h). This immediately relieved her symptoms. She was able to taper the Prednisone to 1 tablet every other day initially, and is now entirely off steroids. The patient did have an episode of what appeared to be the ulnar-tunnel syndrome in February of 1974 and has a minimal persistent rash which is asymptomatic.

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Fig. 1. Faint macular rash on upper inner arm.



Fig. 2. Inner left thigh at the knee showing macular rash.



Fig. 3. Close-up of rash on left thigh; scar of quadriceps muscle biopsy in field.

COMMENT

Many authors have grappled with the varying presentations of the rheumatic disorders and the vasculidities. Frequent overlap of conditions like lupus, dermatomyositis, and rheumatoid arthritis sometimes make a definite diagnosis difficult to make at least at one point in time. This patient presented with a prodrome of non-pruritic macular eruption nearly a year prior to the development of fever. In addition, the rash was in a peculiar distribution not related to sun exposure, namely the medial aspects of arms and thighs. There was a short course of what appeared to be a vasculitis manifested by erythema nodosum on the tibiae which was very brief in duration. The main body of the eruption was macular with nonspecific histopathology and has been notably chronic although it has exacerbated at times of high fever.

The diagnosis of an adult form of Still's disease is based on the fever, splenomegaly (proven at laparotomy), rash, and finally large joint pain especially in the hips without associated muscle weakness. One must seriously consider lupus, however anti-nuclear antibody titres have been repeatedly negative and the rash was not present in light-exposed areas. A strong family history of classical rheumatoid arthritis tends to support the diagnosis of rheumatism although atypical in this patient.

DISCUSSION

Although much has been written about juvenile rheumatoid arthritis in the pediatric age group, very little has been mentioned about the adult presentation of Still's disease. Isdale and Bywaters in 1955 found that only seven adults out of over five hundred that they studied with rheumatoid arthritis had the syndrome of intermittent fever, splenomegaly, lymphadenopathy, and particularly the high sedimentation rate. Ninety-seven percent of the cases showed a rash on the limbs. A small percentage of patients showed a rash on other parts of the body.¹ It was emphasized that the rash was transient, rarely fixed in location, and more prominent with high body temperature. It was emphasized that the rash may precede other manifestations of RA by a period ranging from six months to three years.

In a more recent review, Bujak, et al studied two hundred patients with FUO and within that group

found ten adults who presented a symptom complex which if they were children would have been diagnosed as Still's disease.² Interestingly, all their patients were males with the average age of 24 years whereas in Isdale's study the majority of the adults were women. Bywaters in 1971 reported 14 similar cases which were all women.³ In Bujak's study, all ten patients had significant myalgias especially of the lumbar, cervical, and thigh musculature and polyarthralgias involving the large joints as was seen in the patient described here. In only one of their patients did arthritis lead to deformity and limitation of range of motion. Temporal mandibular joint involvement was not seen in the patients studied by Bujak. Laboratory data is generally non-specific with negative rheumatoid factors, negative anti-nuclear antibody titres, and occasionally elevation of white blood count. Sedimentation rate however is almost always elevated. In Bujak's study, two patients had increased numbers of eosinophils in the bone marrow without peripheral eosinophilia as was seen in the case presented here. The patients described in the literature all responded to the institution of anti-inflammatory therapy, i.e., salicylates, and the judicious use of steroids. Of Bujak's group, only one patient developed deforming arthritis and five of ten patients are on no medications at all suggesting a favorable prognosis.

To date, twenty-five similar cases have been reported in the literature. This patient is offered as the twenty-sixth such case. It has been emphasized by previous authors that the diagnosis of "juvenile" rheumatoid arthritis in the adult is one of exclusion but that evidence of the rash may preclude the necessity of laparotomy in some patients. It is encouraging that as a cause of FUO this condition is at least treatable and has a reasonably favorable prognosis.

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Scalp Avulsion

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Full thickness loss of the scalp is a serious injury. Accidents of this nature were prevalent during the industrial revolution when there was a lack of safety devices to protect workers from the belts and gears of the machines. This is especially true if the periosteum is destroyed as in a burn. The following case is reported as an illustration of the management of extensive scalp avulsion with the periosteum intact.

CASE REPORT

C. S., age 27, was involved in an accident while at work when her hair was caught in a machine and removed a large portion of her scalp. She was brought to the Emergency Floor and examination disclosed this was her only injury. A neurosurgeon, examined this patient, felt there was no intracranial damage, and suggested that a split thickness graft would cover the denuded area. She was taken to the Operating Room and a split thickness dermatome graft was removed from the leg and placed over the defect and held in place with interrupted silk sutures. Five days later the dressing was removed and the graft appeared viable. No further dressing was applied. The graft was exposed. At dis-

charge, it appeared to be taking well and there were no problems. Several weeks later her only complaint was a tightness around the edge of the graft and this was controlled with Darvon.[®] The defect was covered by the use of a wig and in time it was felt that she would be able to cover this with hair growing out around the edges of the remaining scalp.

DISCUSSION

Kazanjian and Webster¹ in 1946 concluded that a full thickness graft is less likely to survive than a split thickness graft on the scalp, and when successful, there has been no hair growth. It is the consensus that a split thickness graft is the method of choice in handling this problem. When the periosteum is destroyed it must be covered, either by local flap, if possible, or if not it has to be covered by a jump flap as soon as possible. If the bone is not covered it will undergo necrosis and be extruded. One method is to drill holes in the outer table and to allow granulation to grow up from the diploë which will accept the split thickness graft. Another²

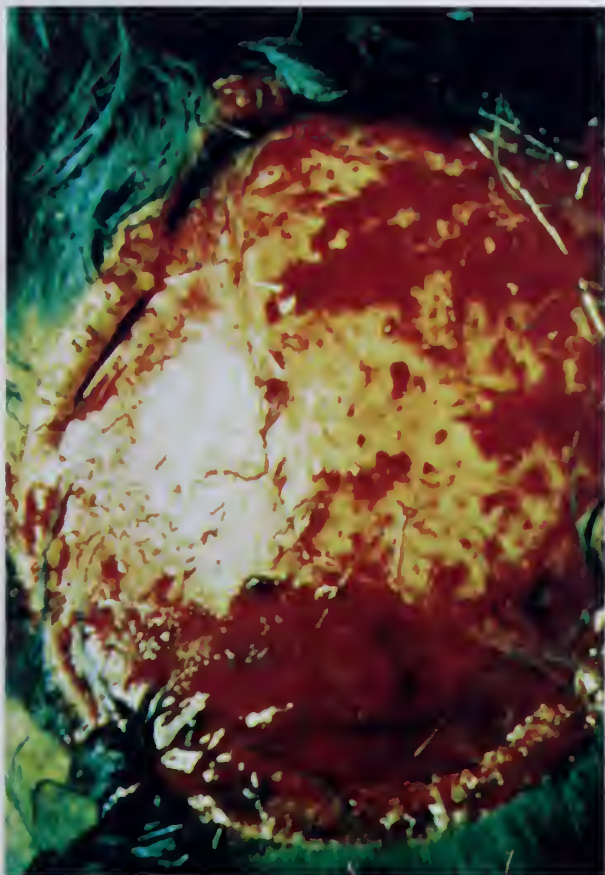


Fig. 1. Photograph of injury at time of admission to the hospital.



Fig. 2. Several weeks later. Coverage is complete.

method is an auto transplant of the omentum with microsurgical revascularization. This provides the necessary immediate covering and then this in turn is covered with a split thickness graft.

CONCLUSION

This case is presented to illustrate a satisfactory method for handling large losses of scalp tissue. A split thickness graft when the periosteum is intact seems to be the method of choice. If the periosteum is destroyed, as in burns and radiation necrosis, stage procedures to cover the defect should be con-

sidered. Omental transplant with microsurgical revascularization is a possibility to be followed by a split thickness graft. To await a granulating bed takes time and this is not without complications.

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addition, the increasing thirst and urinary frequency clearly indicate marked renal function impairment such that the ingested solute load required large volumes for urinary excretion of the salts and metabolic by-products.

The long and the short of it — these patients had

to undergo the long course of delayed diagnosis with weeks of critical hospitalization; whereas, with a greater index of suspicion and sharpened diagnostic criteria, the short course could easily have been pursued.

EDITORIAL

Allied Health Professionals — A Valuable Adjunct

American medicine is in crisis. The quality of medical services in most areas is high; the quantity is not. For most people medicine is catastrophe or, at best, symptom oriented. The private practitioner is overburdened, and for many people the Emergency Ward is the sole medical facility available. An ideal patient-doctor ratio has been postulated at 1:1000. There is no way that this can be approached in the foreseeable future. There are at present 106 medical schools with approximately 47,000 total students enrolled and 11,000 graduating students each year.¹ At the present rate of attrition (death, retirement, etc.) it would take at least 10 years to approach this ratio given a stable population. Our government is committed to a national health scheme in the near future. In an excellent review of the impact of such a scheme, Newhouse and his colleagues² point out that for ambulatory services the demand would increase by a factor of 30 to 75 percent, depending on the plan chosen. This increase would cripple our present ambulatory health care system. Hospital demand is estimated to rise by only 10 to 15 percent. This can be accommodated with present facilities in most places. It is stressed in the article that these are conservative estimates.

The more widespread use of allied health professionals in the delivery of ambulatory care offers a potentially highly effective economic way of dealing with this problem.³ Most primary care physicians recognize that a sizeable percentage of patients seen daily do not require the sophisticated skills of a doctor. Many can be handled by a skillful, sympathetic, medically oriented person. Most of us already utilize our office personnel to some degree in this respect. A wider application involves the use of nurse practitioners, physician extenders, medics, etc. These are specially trained nurses and other health professionals taught to deal with clearly defined ambulatory problems utilizing protocols or algorithms. They have been effectively used in a variety of settings from the hospital emergency ward to the private practitioner's office.⁴⁻¹⁰ These professionals allow access to the health care system for a larger number of people. This is not an innovative idea. It has been used in many countries for years, e.g., Feldshers in Russia, "barefoot doctors" in China, Dressers in Ethiopia and the Nursing Sisters in Central Europe. It is a concept that is receiving greater acceptance in America despite physicians' reluctance because of social and economic factors.¹¹ Certainly the majority of patients readily accept this as shown both by published studies⁴⁻¹⁰ and by my personal experience with two nurse practitioners.

Crisis is derived from the Greek word "krisis" meaning decision. We now face a crisis in the delivery of care and a decision of how we are to fulfill our commitment.

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EDITORIAL

An Open Letter to Internists

Complacency is a comfortable state of mind. Perhaps one of the more useful devices to shatter that state is attendance at various academic meetings of one's profession. Certainly this is a healthy thing to do. Recently I attended a meeting of the Maine Society of Internal Medicine and heard one of the speakers talk in glowing terms about the addition of physicians' assistants and MEDEX personnel to an internist's practice. Clearly no one doubts that much of what physicians have done in the past by themselves has been intrinsically inefficient. Ancillary personnel have proven their value in the collection of review of systems data, in psychological testing, and in the recording of blood pressures and weights, and in the routine administration of instructions and precautions. The physician's time could then be more directed to the somewhat more challenging task of integrating the data with the broader aspects of the patient's lifestyle. However, at this medical meeting, the speaker cited several references which made it plain that physicians' assistants were spending more time with the patient than the physician, especially with regard to history taking. The physician would spend a few minutes with the patient to check some nebulous portion of the history and then move on. This way physicians could see twice as many patients in a day. Apparently the patients were quite pleased with this approach and were easily trained to accept paramedical personnel in this function. It was stated that one P.A. was dictating discharge summaries in the hospital and had applied for limited hospital privileges.

A word of caution here! Education by example has apparently conditioned most patients to expect good medicine to be five minutes with the physician and an hour or more of exotic testing. Physicians' fee schedules are proportional; namely, that several physicians make a good deal of profit on laboratory work and other ancillary procedures, but price their interview with the patient far down the list in value. Third-party payers have fostered this practice by paying readily for procedures, but often denying payment for an adequate interview. As witnessed by the new resurgence of humanism in medical school graduates, the human element in medicine is of utmost importance and this fact should not be forgotten. Those individuals who spend the most time with the patient are those people to whom the patient will relate in every way. If we allow non-physicians to spend thirty minutes or more with the patients, and we ourselves only five, then we will truly jeopardize our ability not only to know our patients but to gather enough intangible and connotative data to make an accurate diagnosis. This is particularly true in internal medicine which is diagnostically oriented. It is hard for one to believe that the physician can derive all the necessary data from a sterile checksheet which does not contain the innuendos and emotional connotations of a face-to-face contact between two human beings. Self-administered checksheets are often ambiguous, especially with regard to review of systems, and may only be of significant help in diagnosis when all the positive findings are checked off, usually indicating a neurotic patient. While an assistant may include only the meaningful data in such a review of systems, he cannot transmit a clear and memorable picture of the whole patient on a checksheet. This can only be gleaned in person.

No one doubts that some physicians' assistants may well have even more sensitivity than some physicians and thereby satisfy the patient's emotional needs. Certainly the patient will have high regard for a sincerely empathetic and interested person no matter what his title. A few patients may even find it easier to speak to a non-physician with regard to family problems. In fact, it is often easier for a physician to allow a third-party to deal with often sensitive and emotional personal issues and reserve himself for integrative functions. This is a dangerous trend. It will soon be possible to have a computer to accurately remember and more efficiently correlate reams of data in diagnostic medicine. The computer can never become a physician and the physician should never become a computer.

What distinguishes the professional from the technician, it seems, is the power of observation. The quality of an initial observation often determines the speed and accuracy of diagnosis. Whether by serendipity or forethought, previous contributions made to medicine have often been by those individuals gifted with the power of accurate observation. Will the physician's assistant in three or four sessions with the patient be able to gather as many truly meaningful data and subtle physical findings as a physician can in one session? I feel that this question has yet to be answered. I as an internist cannot endorse the concept that a physician's assistant should take more than the routine screening history. The diagnostic workup should mandate that a comprehensive history and personal interview be the domain of the physician. In this day and age, we are now being held accountable for time and charges to the patient. I am a firm believer that an accurate diagnosis saves lives *and* money. The initial investment in time to make a correct diagnosis reaps its rewards by saving subsequent office calls and laboratory tests. At least in internal medicine, the person who should spend the most time with the patient should be the physician.

GEORGE E. DAVIS, M.D.
111 Webster Street
Lewiston, Maine 04240

From the Secretary's Notebook

Summary of 1974 Fall Meeting of the M.M.A. House of Delegates

December 14, 1974 at Bangor, Maine

The Fall Meeting of the M.M.A. House of Delegates was held at the Eastern Maine Medical Center in Bangor on Saturday, December 14, 1974, with an attendance of 44 delegates and alternates and seven guests. John B. Madigan, M.D., President of the M.M.A., called the meeting to order, and George W. Bostwick, M.D., Speaker of the House, presided.

1. The Speaker, Dr. Bostwick, announced that he has drawn up some **Rules of Order for the House of Delegates**, which will be reviewed by the Executive Committee at its next meeting on February 1.

2. **Medical School for Maine** — Dr. Robert W. Coon was present to discuss the current status of the school and to ask for re-affirmation of support. He stated that the main question on everyone's mind was funding of the school, but reminds the physicians that this is the responsibility of the legislature to decide. Dr. Coon answered many questions from the floor and emphasized that a vote in favor would be most helpful as this will be coming before the legislature soon. Concern was voiced from some delegates that their county societies has not given them instructions as how to vote. On this matter, Dr. Bostwick reminded them that in this case, one should vote as his conscience directs. A motion was made to postpone a vote until the April meeting of the House, and *lost*. A motion was then made that the House of Delegates favor the present plan for a new medical school in Maine as outlined by Dr. Coon, and this was *approved*.

3. **Blue Cross and Blue Shield 80% UCR Health Insurance** — Present from BCBS to discuss this program were Mr. Richard F. Nellson, President, and Mr. Jerry Merrill who is in charge of claims. Mr. Nellson explained that this program came out of National Blue Shield, and that Maine was obligated to develop such a program. This was approved by the M.M.A. Committee on Health Care Financing, which approves or disapproves all new BS programs. It was then approved by the Maine Blue Shield Board (8 members of this Board are physicians). The State Insurance Commissioner acted on this program early in 1974 and it went on the market 11/1/74. So far, 122 contracts have been sold. Mr. Nellson and Mr. Merrill answered questions

on how this will affect the physicians in the State. Dr. Wood made a motion that we express approval to BCBS and accept their report for information only, and this was *approved*.

4. Dr. Maurice Ross, Chairman of the M.M.A. Committee on Maternal and Child Welfare, was present to express his concern that in some areas, under **Maine's Early Periodic Screening, Diagnosis and Treatment Program (EPSDT)**, exams are being done by non-M.D.'s, and exorbitant fees are being charged. The following resolution was presented by Dr. Ross, and *approved*, with instructions that a copy be sent to Mr. John Fickett of the State Bureau of Medical Care:

WHEREAS, the Maine Medical Association House of Delegates, at its June 1974 meeting, adopted a resolution in favor of greater continuity of medical care for children, warning against the present fragmentation of such care in publicly supported child care programs, and urging the Maine Department of Health and Welfare to place all examination and screening projects in such programs under the direct supervision of the physician or medically supervised clinic responsible for the ongoing medical care of each child; and

WHEREAS, a greater involvement of the private physician in the ever-expanding community health services field is the only guarantee for competent professional standards therein; and

WHEREAS, the State of Maine has failed to respond to and act in accordance with this resolution;

NOW THEREFORE BE IT RESOLVED, that while the Maine Medical Association endorses the goals and objectives of the program, it can no longer support the Early and Periodic Screening, Diagnosis, and Treatment Program as administered at present by the State of Maine; and,

BE IT THEREFORE FURTHER RESOLVED, that the Maine Medical Association endorses a plan of operations, to be sponsored by the Maine Medical Association and the Maine Chapter of the American Academy of Pediatrics and to be administered by Expanded Child Health Services,

Inc., a non-profit corporation, which will:

- a. provide for a central, responsible and continuous role of private physicians in publicly-supported child care services,
- b. eliminate the present fragmentation of preventive child screening and care,
- c. provide for high professional standards governing the use of para-professional personnel (such as those recommended by the American Medical Association and the American Academy of Pediatrics), and detailed evaluation of such services,
- d. assure lower cost, less administrative expense and less paper work for the physician,
- e. result in higher productivity of the medical profession by enabling a much larger number of children to be served in a higher quality program.

5. Report of Delegate to AMA — Dr. Robert E. McAfee reported on the recent meeting and stressed that the AMA is in dire financial difficulty. A \$60 mandatory assessment of AMA members for 1975 has been approved. The House of Delegates spent a good part of the convention discussing this predicament. The second most important item of discussion was malpractice insurance. No answers to the problem developed, but it has been given #1 priority. Among other items discussed and reported by Dr. McAfee were AMPAC, acupuncture and weight reducing clinics.

6. Items presented by the county medical societies — The following resolutions were presented by Dr. John Davy of Cumberland County:

Cumberland County Medical Society #1

WHEREAS the physician members of the Cumberland County Medical Society represent some three-hundred of the members of the Maine Medical Association, or approximately 30% of the membership, and

WHEREAS proportionate representation is an important philosophy and principle for organizations to adhere to,

BE IT RESOLVED that the Maine Medical Association shall structure the Committee on Health Care Financing of the Council on Medical Services, according to the principle of proportionate representation of membership.

Dr. Wood made a motion that this be referred to the Executive Committee for appraisal and report back to the House of Delegates in April, and this was approved.

Continued on Page 87

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonsfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 25 mg of diphenoxylate HCl with 0.025 mg of atropine sulfate. Liquid, 25 mg of diphenoxylate HCl and 0.025 mg of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml (total capacity, 2 ml.) accompanies each 2-oz bottle of Lomotil liquid.

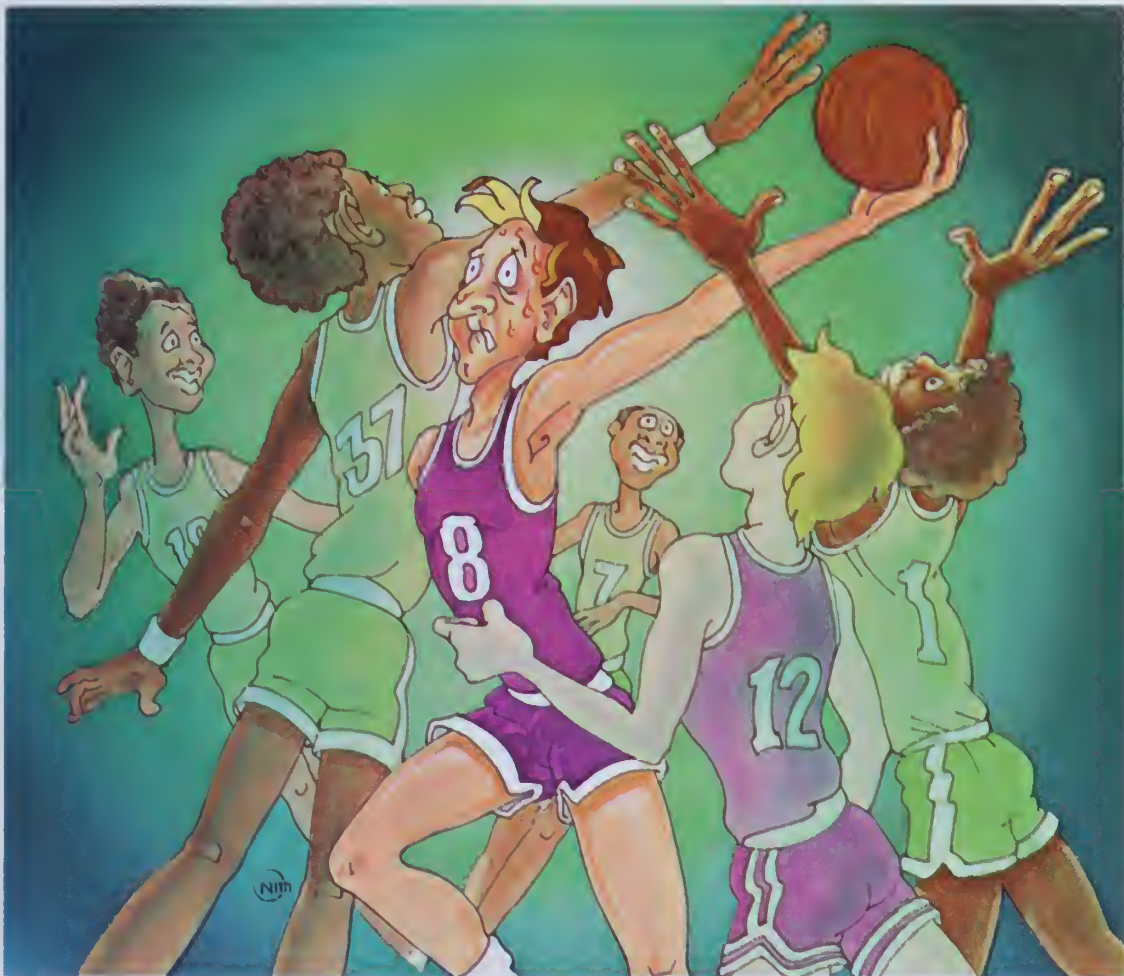
SEARLE

Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to
G. D. Searle & Co.
Medical Department, Box 5110
Chicago, Illinois 60680

454 R

When diarrhea has his number...



Lomotil puts him back in the game.

Physicians and patients both want prompt control of the symptoms of diarrhea. A rapid, uncontrolled loss of fluids and electrolytes can cause a medical crisis, particularly in children, and in patients who are seriously ill, or in people who are badly undernourished.

Lomotil usually stops diarrhea promptly. This rapid action halts the emergency aspect of diarrhea

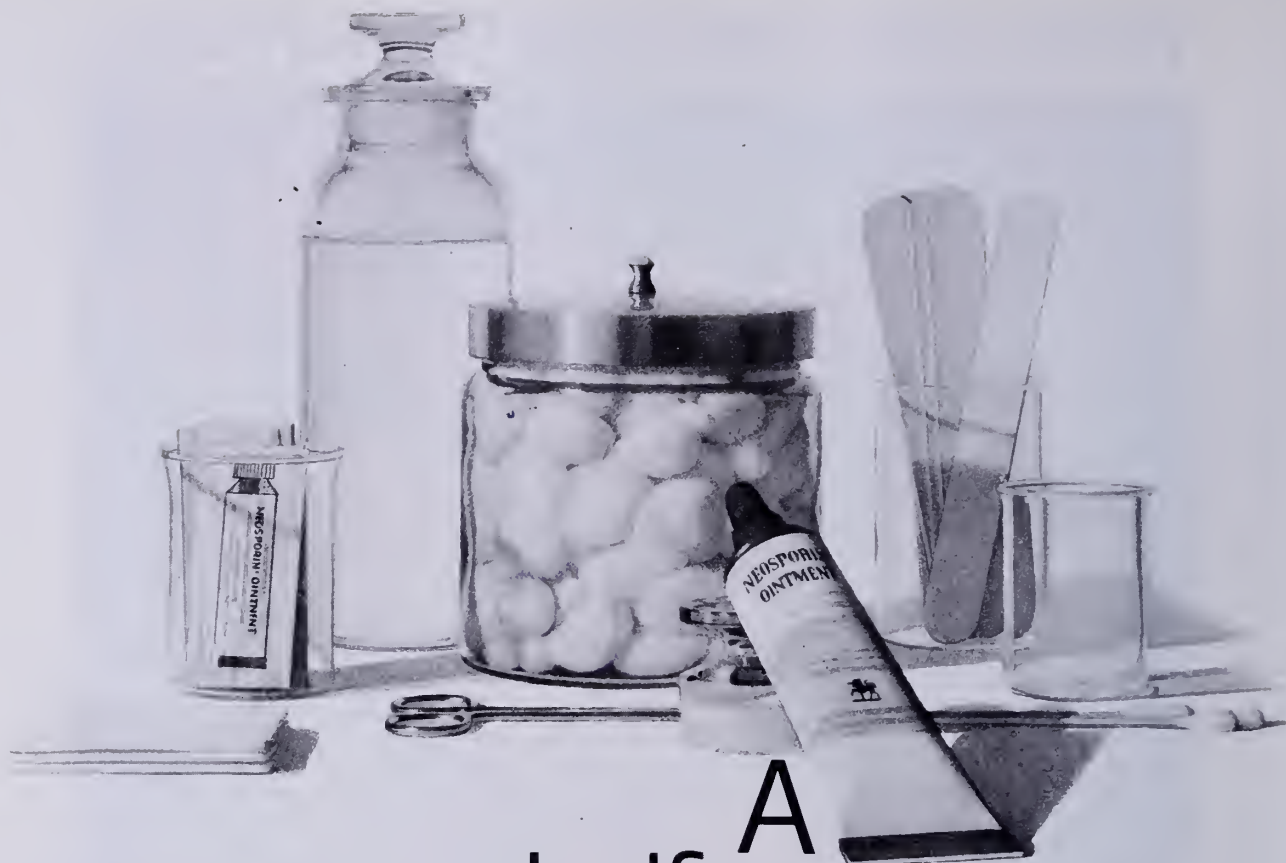
and is comforting and reassuring to the patient. Electrolyte and fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate antibiotic therapy should be given along with Lomotil.

Lomotil has few side effects, and those that do occur are generally mild.

Lomotil[®]
TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:
diphenoxylate hydrochloride 2.5 mg.
(Warning: May be habit forming)
atropine sulfate 0.025 mg.

Usually stops diarrhea promptly.



A half-ounce of prevention

Use it to prevent a topical infection. Or to treat one that's already started. In either case, it's good medicine. Whether for lacerations, burns, open wounds, IV catheter or surgical aftercare. Neosporin® Ointment provides broad antibacterial coverage against common susceptible pathogens. And since it contains three antibiotics that are rarely used systemically, the risk of sensitization is reduced. Neosporin Ointment. A half-ounce of prevention. Also available in a full ounce of prevention and in convenient foil packets. Neosporin Ointment carried on Apollo and Skylab missions.

Neosporin® Ointment (polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs.
In tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically*, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where

absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PM



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities.

Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently — both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F CO.
Carolina, P.R. 00630
Subsidiary of
SmithKline Corporation

KEEP THE HYPERTENSIVE PATIENT ON THERAPY KEEP THERAPY SIMPLE WITH **DYAZIDE**[®]

Each capsule contains 50 mg. of Dyrenium[®] (brand of triamterene) and 25 mg. of hydrochlorothiazide.

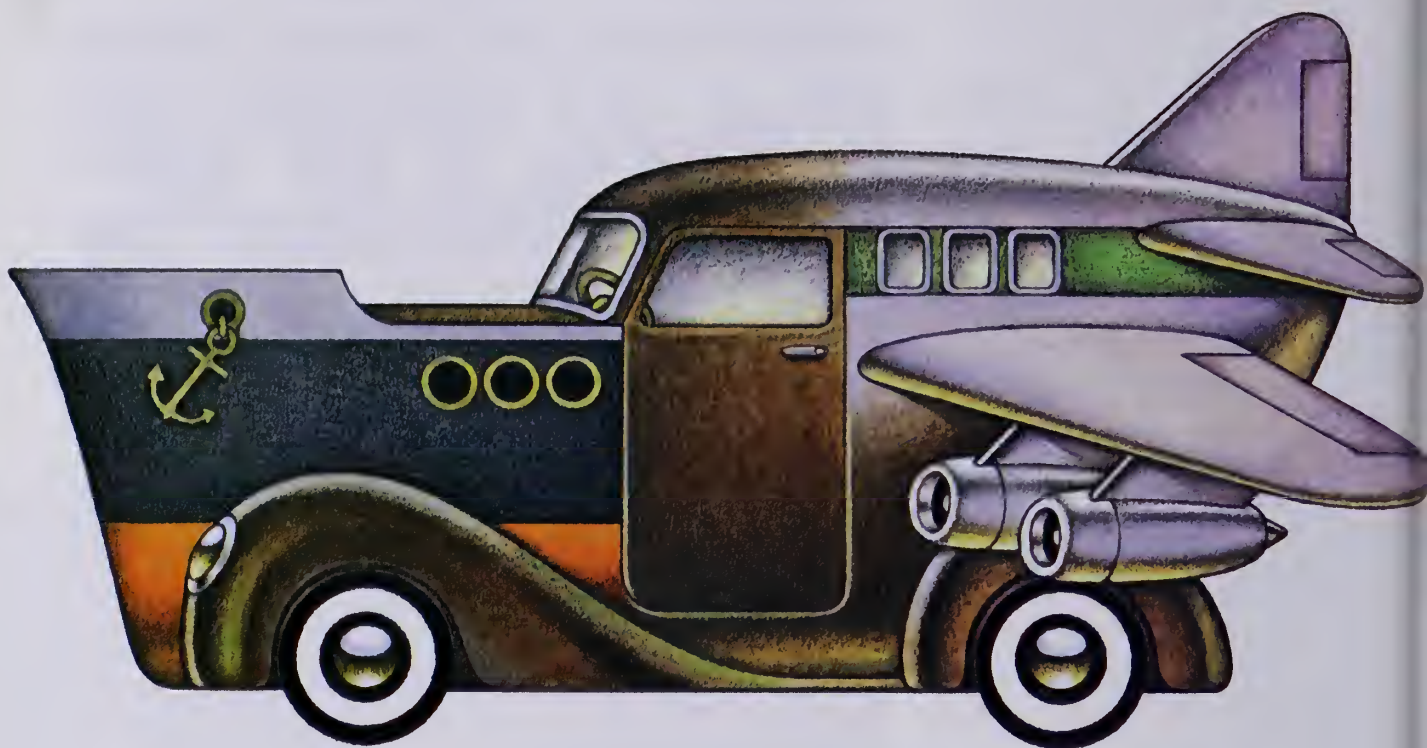
Trademark

Neither inconvenient potassium supplements
nor special K⁺ rich diets needed as a rule.
Just 'Dyazide' once or twice daily for maintenance.



Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP



On land, sea, and in the air...

Up to 24 hours of effective control with a single dose...in nausea, vomiting and dizziness associated with motion sickness.

Dosage: 25 to 50 mg. 1 hour before travel.

Available on prescription only.

BRIEF SUMMARY OF PRESCRIBING INFORMATION
CONTRAINDICATIONS. Administration of Antivert during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did

not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

ROERIG 
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert®/25 Chewable Tablets
(meclizine HCl) 25 mg.
for motion sickness

Cumberland County Medical Society #2

WHEREAS physicians of the Maine Medical Association are members of the Board of Trustees of Blue Cross/Blue Shield, and

WHEREAS this Health Insurance Organization is playing an increasingly important role in the financing of medical care in Maine, for both inpatients and outpatients, and affecting the professional lives of Maine physicians, and

WHEREAS there is at present, no limit on the term of those physician board members on the Blue Cross/Blue Shield board, and

WHEREAS there is a need for wider participation by Maine Medical Association physicians, Blue Cross/Blue Shield in the activity of the Blue Cross/Blue Shield so that all ages, elements, and philosophies of physicians in the State can be represented,

BE IT RESOLVED that the Maine Medical Association recommend to the Board of Blue Cross/Blue Shield (AHS) the terms of physician board members be limited to terms of 3-5 years, with the exception that the physician Executive Director of the Maine Medical Association continue to serve as a board member without a fixed term of office.

A motion was made by Dr. Wood that this be referred to the Executive Committee and it was *approved*.

7. Committee reports —

a) *Care of the Disadvantaged* — Dr. Bostwick, Speaker of the House, reported that the Executive Committee decided at its meeting today to refer this report to their next meeting for recommendations.

b) *Recruitment, Aid & Placement* — A list of recipients of aid from the Maine Medical Education Foundation for the present school year was given to each member of the House, and Dr. McAfee, Chairman of this Committee suggested that physicians contact students in their own area to let them know of our interest in helping them.

c) *Continuing Education* — Given to each member of the House for future reading were the following: Sample copy of Continuing Medical Education Activity Report that will be mandatory in 1975 for membership in the M.M.A.; minutes of the CME Committee meeting on 10/17/74; report of the AMA 4th Biennial Conference on CME for the State Medical Societies and Specialty Societies; and in accordance with the House of Delegates' instructions to this committee, copy of a proposed budget for the CME Program of the M.M.A. Major expense involved in this program is the accreditation

of CME programs in the State. A decision will have to be made as to how to pay for this expense, and *each member of the House is asked to bring back their opinion on this proposed budget at the April meeting.*

d) *Peer Review* — Dr. Chamberlin, Chairman, reported that the committee has been meeting and keeping up to date with PSRO which now has 645 Maine members signed up. The Maine PSRO has submitted a proposal for operational status. Progress in PSRO is reported each month in *The Journal of the Maine Medical Association*. Dr. Chamberlin also called attention to new Utilization Review Regulations (*Legislative Roundup* copy, 12/6/74, re these regs, given to each member of the House).

8. Other —

a) **Malpractice** — Dr. Hanley noted that the June House of Delegates instructed the M.M.A. office to conduct a survey on malpractice, but in working on it, it has become obvious that it is an exercise in futility. Dr. Richard Swengel, Secretary of the Androscoggin County Medical Association, reported that they did such a survey — it was expensive, there was no way to authenticate the figures and what do you do with it? A motion was made to rescind the request for the malpractice survey, and it was *approved*.

The number of claims is doubling, Dr. Hanley said, and reported on some figures obtained from companies on malpractice experience in Maine. Some individual malpractice insurance contracts are not being renewed, even though those individuals have not had a claim against them; those that are being renewed at usually at a much higher premium, and are in class 1 & 2.

b) Although the **1974 Pension Reform Act** raised allowable limits under the Keogh Law from \$2,500 to \$7,500, Maine has yet to enact this change in their tax laws, and until they do so, physicians in Maine could be penalized for contributing more than the old \$2,500 limit to their pension plans.

c) **Consumer Credit Code** is a new law, but amendments are in the works. Advice to physicians is that they have no finance charges, and accept payments in 3 or less installments.

d) It was reported that the Androscoggin County Medical Association **resolution re psychiatric care**, referred to the Executive Committee in June by the House of Delegates, has been discussed by the E. C. and is currently tabled, pending the outcome of an investigation of a related matter.

e) A newspaper article reporting an interview with Mr. Mark Knowles, Director of the State **Comprehensive Health Association**, has caused great concern among physicians as it indicates the possibility of closing many small hospitals in the State.

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HEALTH COSTS KEY ISSUE AT WHITE HOUSE CONFERENCE

At the recent White House Economic Conference on Health and Other Social Services, James D. Knebel, National Association of Blue Shield Plans executive vice president, expressed concern over inflation and medical costs and pledged the organization's cooperation in helping to contain costs.

Cautioning against furthering inflation, Knebel urged government leaders to maintain close scrutiny on the cost of Federal programs, and to give careful consideration to the short and long-term effects of various legislative proposals.

The Blue Shield leader suggested that inflation — especially in health care — must be viewed as a social and political phenomenon rather than purely an economic one. Before resolving problems in the health care sector, he said certain truths must be put in perspective:

- the health care sector is continually expanding because of advances in medical technology and the social decision to make use of them. This results in increases in the price and utilization of health care.
- the shift over the years in the financing of health care from patient to third-party payers has increased the demand for health care and has caused inflationary pressures. Presently, two-thirds of the health care dollar is financed through third parties.
- the desire for additional and expanded benefits such as coverage for dental care has economic consequences in terms of higher costs and increased use of these benefits.

In a background paper distributed at the conference, government economists warned that national health expenditures are expected to jump about 14 percent, from \$105 billion in 1974 to over \$120 billion in 1975. Due to this increase, personal out-of-pocket expenses will increase eight percent, from about \$30 billion this year to \$32 billion in 1975.

According to the paper, health insurance premiums will also reflect the rise. A family paying \$400 in 1974 will pay over \$50 more for the same policy next year.

Medicare expenditures are expected to increase by over 25 percent from \$11.3 billion in 1974 to about \$14.3 billion in 1975, which could adversely affect prepaid group health plans.

Knebel said, "Blue Shield has been living with these facts of life, and has faced them by constantly strengthening its cost containment efforts.

"We are working to restrain physician fee increases within reasonable levels through our Usual, Customary, and Reasonable charge programs. While monitoring changes in physician fees," he added, "we are also carrying out a campaign to keep them within reason."

Knebel said the Cost of Living Council's "inflation watch" has merit. "The government alone has the power to make certain basic decisions to combat inflation," he said.

"We urge that government take action by increasing taxes, continuing stringent monetary policies, reducing Federal and state budgets or keeping them under careful control and balancing the budget," stated Knebel.

News, Notes and Announcements

Congratulations and Best Wishes to the New Lincoln-Sagadahoc County Auxiliary Organized February 3, 1975 at the Bath Memorial Hospital.

Infection Control Seminar

The Bureau of Health, the Maine Hospital Association, Kennebec Valley Regional Health Agency and Northern Maine RAISE are co-sponsoring a two-part infection control seminar to be held at the following locations:

	Part I	Part II
Lewiston		
Bates College	March 31-April 1	May 5 and 6
Bangor —		
Eastern Maine		
Medical Center	April 3 and 4	May 8 and 9
Presque Isle —		
University of Maine at P. I.	April 7 and 8	May 19 and 20
Registration forms will be mailed to prospective participants by March 1st.		

All disciplines from Maine's health care facilities, as well as representatives from those agencies involved in post-discharge medical care, are invited to attend.

54th Annual Meeting of the N.E. Hospital Assembly, Inc.

In an era when traditional boundaries between disciplines are crumbling and evaporating, the 54th annual meeting of the New England Hospital Assembly Incorporated, Tuesday through Thursday March 25-27 at Boston's Sheraton-Boston Hotel and John Hynes Veterans Auditorium, holds a special allure for physicians.

A host of programs concern themselves with topics of direct interest to doctors, and others address matters that have or soon will impact the medical profession.

There is no admission or enrollment fee for the programs. One need only register in the Hynes Auditorium lobby, receive a badge and program booklet, and then set out in pursuit of whatever topic is of personal interest.

A total of 14 general sessions will be presented during the three day educational conference. Here are some whose content have special relevance to medical practice today and tomorrow.

"The Myth — And Cost — Of Defensive Medicine" will be explored at 2:30 on Thursday March 27, in Room 104 of the Hynes Auditorium. Speaking is E. James Potchen, M.D., associate dean of Johns Hopkins School of Medicine. He intends via "systems dynamics" to show the inflationary effect of defensive medicine upon hospital and medical costs. Particularly, he'll explore the pro and con of defensive medicine, ways to cut malpractice cost, the preservation of diagnostic intervention, and the limits of health care cost. He also will detail the concept of systems dynamics.

"Emergency Department: Critical Care Center, Primary Care Clinic or Both," earns scrutiny from two experts on Wednesday, March 26 at 10:30 a.m. in Room 104 of Hynes Auditorium. David R. Boyd, M.D.C.M., director of the Division of Emergency Medical Services, U.S. Dept. of H.E.W., Public Health Service, Washington, D.C.; and Nora Piore, Professor of Health Economics, Columbia School of Public Health share the platform. They will examine provider responses and legislative directions in meeting public needs for emergency services and public demands for instant primary care. They also will discuss: who comes to emergency rooms and why, hospital responsibilities and roles in the providing of emergency services and primary care, roles of non-hospital providers, and the different approaches in different settings, such as rural, urban medical

center, community hospital and so on.

Sessions also treat "The New Federal Planning Legislation" and its numerous impacts upon all health professionals and their patients (2:30 p.m., Tuesday March 25); "PSRO: Implications for Nursing and Allied Health Professions" (10:30 a.m., Wednesday March 26); "Death and Dying" (2:30 p.m., March 26); "Regulation; How To Survive Fiscally" (2:30 p.m., March 26); "National Health or National Health Insurance?" (10:15 a.m., Thursday March 27); and "Peer Review — Nursing and The Allied Health Professional" (10:15 a.m., March 27).

In addition to the general program sessions, the annual meeting also features two floors of exhibits in Hynes Auditorium. They array the latest technology, techniques and products of the health sciences in one convenient, easy-to-visit location.

A booklet describing the entire 54th New England Hospital Assembly Incorporated annual meeting is available by writing: Mrs. Jean Quigley, 76 Crest Avenue, Chelsea, Mass. 02150.

State of Maine Department of Health and Welfare Division of Child Health Clinic Schedule — 1975

Children's Development Clinics

Lewiston — Central Maine General Hospital

8:30 a.m.: Mar. 10, 24, Apr. 14, 28, May 12, June 9, 23, July 14, 28, Aug. 11, 25, Sept. 8, 22, Oct. 27, Nov. 10, 24, Dec. 8, 22

Waterville — Thayer Hospital

8:30 a.m.: Mar. 5, 19, Apr. 2, 16, 30, May 7, 21, June 4, 18, July 2, 16, 30, Aug. 6, 20, Sept. 3, 17, Oct. 1, 15, 29, Nov. 5, 19, Dec. 3, 17, 31

Pulmonary Disease

August 24-27, 1975. Second Annual Seminar, Topics in Pulmonary Disease. National faculty including Barry Fanburg, M.D., Hans Weill, M.D., John F. Murray, M.D., and more. Twenty-one hours of Category I credit available. Colby College/Thayer Hospital, Waterville, Maine. Inquiries to R. H. Kany, Director, Special Programs, Colby College, Waterville, Maine 04901.

Maine Poison Control Center 871-2381

Emergency Poison Information Service
for physicians in Maine.

For non-emergency information,
please call on weekdays between 9:00 a.m. and 2:00 p.m.
The Poison Control Center is located in the
Emergency Division of the
Maine Medical Center.

State of Maine Board of Registration of Medicine Physicians Licensed to Practice Medicine and Surgery in the State of Maine Through Reciprocity

Anderson, Larry G.; Chandler, Richard C.; Cloutier, Elmer G.; Cohen, Samuel M.; Dunst, Jerome; Hakami, Taghi; Head, Roger C.; Holt, William S.; Khoury, Nicholas F.; La Marche, Paul H.; Markus, Ivan P.; McKnight, Mary J.; Menges, John C.; Metz, Joseph R.; Millan, Angelo P.; Moyes, Karen R. F.; Murakami, Noboru; Pezzuti, Roger T.; Reddy, Venkatesha G. S.; Reed, Stephen D.; Rowell, Harlow B.; Silverman, Stephen D.; Stock, Donald H.; St. Peter, Dennis A.; Swarr, James H.; Thompson, Edward C.; Ward, James S.; Wise, Robert I.; and Zientara, Marie T.

County Society Notes

LINCOLN-SAGADAHOC

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held on December 17, 1974 at the Ledges Inn in Wiscasset, Maine.

Twenty-eight physicians attended the meeting, which was called to order at 8:40 p.m. by the President, Dr. Peter A. Evans. The minutes of the November meeting were accepted as read by the Secretary.

Dr. Elihu York reported matters discussed at the Interim Session of the M.M.A. House of Delegates held three days previously in Bangor. Subjects included PSRO rules and reporting of continuing medical education efforts.

Dr. Carl R. Griffin, Jr. spoke about HR 16204, regarding a controlled planning system to regulate health services in the states.

Dr. Richard C. Leck enlarged on the two previous reports. He reported that the medical malpractice insurance problem is

reaching crisis proportions. The State laws governing consumer credit dealings were abstracted, and the implications were hotly discussed.

Dr. Henry A. Hudson moved that in the future the scientific program be presented before political discussions. The motion was seconded; the vote was seven in favor and seven against. Dr. Hudson then withdrew his motion.

The Board of Censors recommended that Drs. Alex Norzow of Brunswick and Richard Cote of Bath be inducted into active membership in this Society. The members present voted unanimously to accept these recommendations.

There was no old or other new business. Dr. Evans appointed Drs. Griffin, Belknap and Dougherty as the Nominating Committee, to bring in a slate of proposed officers at the January meeting.

Dr. Robert S. Galen then introduced Dr. Philip Crichton who spoke on Angiography.

GEORGE W. BOSTWICK, M.D., *Secretary*

FROM THE SECRETARY'S NOTEBOOK – Continued from Page 87

A resolution to censure Mr. Knowles, and request his resignation, was amended to express disapproval of his expressed views. After much discussion, this was *defeated* and the M.M.A. President instructed to write a letter to the President of the State CHA, asking for some clarification of their stand on this and expressing the difficulties that have arisen out of the appearance of the article.

9. **Spring Meeting of the House of Delegates** — Saturday, April 12, 1975 in Waterville at 2:00 P.M. (meeting of the Executive Committee at 10:00 A.M.)

10. Adjourned at 5:15 P.M.

PATRICIA A. BERGERON

Secretary-Treasurer, M.M.A.

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The Journal of the Maine Medical Association

Volume Sixty-six

Brunswick, Maine, April 1975

Number 4

NEW ENGLAND CANCER SOCIETY

The various papers on the following pages of this issue of the Journal were presented at a meeting of the New England Cancer Society held at the Maine Medical Center on October 5, 1974.

The New England Cancer Society is a scientific organization which recognizes that to be effective "in humanitarian service, all useful methods must be made available to those in need, it becomes our further purpose to promote adequate distribution of agencies for bringing the best of technical skills, equipment, and information into the service of all sufferers from these diseases.

As a primary means to further the above objectives, this association shall serve to bring together workers in the various fields of cancer investigation, control and therapy for exchange of information among its members. The members then may convey such information to the medical practitioners in the locality."

The organization was founded in 1939. The first meeting was held at Pondville Hospital, Walpole, Massachusetts. Since then the society has held continuous biannual meetings, one of which is in New England and the other outside the New England states. The society has enjoyed the enviable experience of accepting invitations from the leading cancer research and therapy institutions throughout the United States, Canada and Europe. In 1960 the society accepted and attended its first overseas meeting, held at the Royal Marsden Hospital, Westminster Hospital, Middlesex Hospital, London, England. The meeting was engineered by the secretary, Dr. Gerald Garcelon, and was so successful and the reception so magnanimous that subsequent trips have been made to the Radiumhemmet, Stockholm, Sweden, Radium Center, Copenhagen, Denmark, Institut Gustave Roussy and Foundation Curie, Paris, France, The Netherlands Cancer Institute, Amsterdam, Holland, St. Bartholomew's and Royal Marsden Hospital (Surrey Branch), London, England, and St. Luke's Hospital, Dublin, Ireland.

These overseas sessions have been highly worthwhile and the dialogue between our membership and our hosts has been instructional, beneficial, and sometimes constructive to both. The same comments are also applicable to our visits to the many prestigious institutions in this country and Canada.

Throughout the years the membership and officers have included many eminent scientists, surgeons, radiologists, radio-therapists, pathologists, and oncologists, who devote the major part of their endeavors to cancer programs and management.

It has been thirty years since the Maine General Hospital hosted the New England Cancer Society. Since that time, the hospital has grown in stature and as a result of the expertise and experience of its staff is now able to present an attractive program of interest and value to the membership. It was the opinion of the committee arranging this program and the editorial staff of the Maine Medical Association that these contributions would be of interest and value to the membership of the Maine Medical Association.

JOSEPH E. PORTER, M.D.
Maine Medical Center
Portland, Maine 04102

Soft Tissue Sarcoma — Some Observations on Diagnosis and Treatment

ROBERT E. MCAFEE, M.D.*

It is a well recognized medical axiom that the rarer the lesion or disease, the greater the number of experts in the field. Because soft tissue sarcomas are indeed rare — comprising only 0.5 percent of all malignancies — and because most physicians think they have seen at least one case of each of the different varieties of sarcoma that exist, one might then define an expert in this field as one who has managed at least *two* cases of soft tissue sarcoma. Unfortunately there are more than 20 types of soft tissue sarcomas, each with distinguishing histologic and different biologic behavior and with varying tendencies for local infiltration and distant metastases. It is for this reason that the individual who provides primary therapy for these lesions should be able to offer the best chance for cure. The better and earlier recognition of these lesions and their appropriate therapy is the aim of this presentation.

DIAGNOSIS

Although some changes have occurred in the treatment of soft tissue sarcomas in recent times, aids to the clinical diagnosis of these lesions have not improved significantly. A keen clinical awareness of the possibility of soft tissue sarcoma probably accounts for the more prompt recognition of this problem than any other single test. Laboratory procedures in general have limited value in the diagnosis of soft tissue tumors. Soft tissue x-ray or angiography are usually unnecessary except in the retroperitoneal area. The possible x-ray appearance of the stippled x-ray calcification seen in a synovial sarcoma might represent the only exception to this rule. There remains no good hematologic test that would aid in the diagnosis of these lesions.

For the most part sarcoma has become evident as painless soft tissue masses that grow and sometimes become symptomatic because of their size. Localized neuralgias, ischemia and even paralysis may occur because of compression on adjacent nerve structures. Rarely do the systemic effects of weight loss and general malaise alert one to the possibility of underlying sarcoma. Although paraneoplastic syndromes have been described mostly having to do with carbohydrate metabolism and subsequent hypoglycemia, these syndromes are for the most part associated with large bulky tumors which are

obvious to even the most casual observer. It remains then that biopsy — excisional if the lesion is small or incisional but generous when the lesion is large remains the hallmark of appropriate diagnosis for soft tissue sarcomas. The difficulty in identifying specifically these lesions by frozen section diagnosis is readily apparent to all pathologists and increasingly apparent to most surgeons. It is felt that whereas treatment may significantly be altered by a different histologic diagnosis that appropriate permanent sections be utilized for this purpose whenever possible.

SPECIAL CONSIDERATIONS

Many classifications have been proposed to help identify tissue origin of most of the soft tissue sarcomas. That which remains most useful is by Stout,¹ however, although classifications make it easier to consider ultimate therapy, it in no way is immediately helpful to the operating surgeon when faced with initial form of therapy. It has been estimated that fibrosarcomas, liposarcomas and rhabdomyosarcomas together comprise approximately 80 percent of all soft tissue sarcomas seen today. This has been true in the experience of the author and is corroborated by other studies and literature.^{2,3}

Fibrosarcomas are perhaps the most common of all sarcomas and occur slightly more commonly in males in the 20 to 50 year age group. They have, however, been described in infants as well as the octogenarian. These tumors are generally grayish white in color, usually firm and homogenous in nature but most specifically are pseudoencapsulated despite their frequent appearance of being entirely encapsulated and easy to enucleate if one is not aware of this histologic pattern. Special forms of fibrosarcoma including the dermatofibrosarcoma which may occur on the trunk or on the scalp and as being somewhat purplish or polypoid in appearance and the desmoid type of fibrosarcoma, a sometimes indolent but occasionally aggressive form of the tumor occurring either in the abdominal wall or on the extremities are special forms of fibrosarcoma, the most specific details of which the reader is referred to Pories.⁴

Liposarcomas are the second most common tumor and it is particular to note that they rarely arise from preexisting lipomas but almost always

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begin as denovo tumors. These tumors may be quite large with multiple convolutions occasionally even suggesting the anatomic appearance of cerebral convolutions. There may be adjacent satellite nodules around most liposarcomas and indeed there is great histologic variation from the rather benign appearing well differentiated myxoidliposarcoma to the very pleomorphic and extremely anaplastic form of the tumor. Within this framework alone, survival figures in the order of 60 percent for the rather benign and differentiated type will be significantly decreased to approximately 10 percent in the more aggressive type with similar therapy.

Rhabdomyosarcomas are usually divided into three separate entities: the adult pleomorphic type arising most frequently in the extremities usually in large muscle groups; the embryonal rhabdomyosarcoma occurring primarily in children and young adults and found in the extremities and associated with increasingly severe pain sometimes even anteceding the appearance of the tumor; and thirdly, the embryonal rhabdomyosarcoma which is polypoid or grape-like in appearance and again found primarily in children and most common in the head and neck, genitourinary tract, orbit and nasopharynx and carrying an extremely poor prognosis.

OTHER SARCOMAS

Synovial cell sarcoma also arising within the vicinity of ligaments and tendon sheaths but rarely within direct contact with joint synovia itself are also frequently anteceded by localized and severe pain in the area of the tumor before the tumor may become apparent. Tumors of vascular origin including Kaposi's sarcoma, angiosarcoma as well as the lymphangiosarcoma and fibrous histiocytoma are other sarcomas to be appreciated and the reader is referred to more definitive works for their specific characteristics.⁵

TREATMENT

Adequate wide excision is the surgical treatment of choice for patients with soft tissue sarcomas. Early inadequate excision increases the incidence of local recurrence significantly and for the most common sarcomas five-year survival figures are reduced by as much as 50 percent with a single local recurrence.

A significant breakthrough in adjunctive therapy of patients with soft tissue sarcoma of an extremity was made by Suit and associates⁶ who first pointed out significant improvement in survival figures with the use of radical dose radiation therapy when combined with some form of surgical excision of the tumor. Although this was proposed as an alternative to major amputative surgery, the results of this form of treatment compare very favorably with surgical therapy alone of even the most radical type. The re-

finer technique of not beginning therapy until the surgical wound is completely healed and allowing a single strip of skin not to be radiated to prevent cicatricial scar and excluding if possible the delicate skin overlying the patella and tibial shin and treating all fields each day to the radiation dose of 6300 to 7000 rads for five days a week for six and a half to seven weeks seems to have minimized complications and provided more functional results.

It would now seem that patients with soft tissue sarcomas arising below the elbow or below the knee who might formerly have been candidates for radical extirpative surgery or amputation would best benefit from wide local excision and radiation therapy. More proximal lesions will still require significant muscle group excisions and/or amputative excision in order to improve survival figures. Although most soft tissue sarcomas metastasize by the hematogenous route with the lung being the most common site of metastases, 7 to 10 percent of the more common sarcomas may show regional lymph node involvement. For this reason, when tumors are in reasonably close proximity to these nodal areas, they should be encompassed in the surgical extirpation.

Although we have had a small experience with isolation perfusion of the extremity with these lesions, our objective response rate has not been high and for this reason until others have identified a more specific chemotherapeutic agent we have not continued this technique as a significant adjunctive form of therapy. As far as chemotherapy in general is concerned, until the recent use of Adriamycin[®] for some soft tissue sarcomas, no significant objective response rate has been noted with any of the more commonly utilized drugs. It is again for this reason that the onus of appropriate therapy still relies upon the operating surgeon who first is faced with a soft tissue sarcoma to remove as much of the bulk of the tumor as can be done consistent with good surgical technique and minimal morbidity.

SUMMARY

The basic principles therefore of management of soft tissue sarcomas are as follows:

1. The accuracy of clinical diagnosis of these tumors is extremely poor.
2. Only by proper histologic examination of a biopsy specimen can an accurate diagnosis be achieved.
3. Laboratory procedures have limited value in the diagnosis of soft tissue tumors.
4. The first treatment offers the best chance for cure.
5. Adequate wide excision remains the hallmark of treatment for patients with soft tissue sarcomas.

Continued on Page 96

Aspiration Biopsy of Solid Breast Masses

100 Consecutive Cases

GEORGE F. SAGER, M.D.* and LOUIS N. TAXIARCHIS, M.D.**

We all must acknowledge that significant emotional trauma is involved when a woman enters the hospital for treatment of a lump in her breast. "Is it a cyst?" "Is it a benign solid tumor?" "If it is cancer what operation will the doctor employ to treat it?" Most cysts can be identified and treated in the office by the aspirating needle and the patient is then reassured, and hospitalization avoided. If the mass is solid, an aspiration biopsy may give enough information to prepare the patient for the diagnosis of cancer, and give her the privilege — yes, even the right — to discuss the type of treatment to be used in her particular case.

We are not discussing the cytologic study of fluid aspirated from cysts. Nor are we discussing the histologic study of cases of tissue removed by large bore biopsy needles (Vim-Silverman etc.). We are discussing the aspiration of tissue juice and small flecks of tissue through a small bore (20-22 gauge) needle and smearing this on a slide for preparation and study as in a Pap smear. This method of studying breast tumors is not new. The Memorial Hospital¹ for Cancer and Allied Diseases in New York has been utilizing it satisfactorily for about 40 years. Dr. Zajicek^{2,3,4} of Stockholm, Sweden, has accumulated a vast experience and his results have been widely accepted in Europe^{5,6,7} but until quite recently has generated only sporadic interest in this country.^{8,9}

METHOD

The breast mass is immobilized between two fingers and the chest wall and the overlying skin "sterilized." Using a disposable syringe with a 20, 21 or 22 gauge needle, the needle is quickly thrust through the skin without local anesthesia. After the point of the needle is within the mass, strong suction is applied to the syringe and the needle passed several times in different directions through the mass. The suction is then released slowly and the needle and syringe removed from the breast. If negative pressure is not completely released before withdrawing the needle, when it comes out of the skin, air rushing through the point of the needle sprays the juice and tissue particles onto the inside of the syringe barrel where they are lost. If performed cor-

rectly, the entire specimen usually remains within the lumen of the needle. The needle is removed from the syringe and air is drawn into the syringe. The needle is reattached and the juice and tissue particles gently blown from inside the needle onto a microscopic slide. Special frosted slides may be used to enhance adherence of tissue to glass, but we usually do not find this necessary. The smear is immediately fixed, as with any Pap smear, to prevent artifacts caused by air drying. The slide is then sent to the cytology lab where it is stained and examined. The cytology slip should contain some clinical information and the clinical impression of the person taking the biopsy.

MATERIAL

In February 1973, this study was initiated by one physician, and after one year the experience was adequate to make the test generally available. In February 1974, other physicians began to utilize the procedure and by September 1974, 100 consecutive cases had been studied from 17 physicians. All cystic lesions of the breast, and all aspirations of other organs (thyroid, parotid, lymph nodes) were excluded from this study.

RESULTS IN LITERATURE

Memorial Hospital has had 200-250 cases per year for over 40 years. Their study¹ covering a recent two-year period showed 14% false-negative (includes unsatisfactory smears) and 0% false-positives. All positive smears had mastectomy without frozen section biopsy.

From the Radiumhemmet in Stockholm,³ a series of 2,200 cases were reported with 8-12% false-negative and 0.1% false-positive.

Dr. Rajcic⁷ reports from Zagreb, Yugoslavia a 16-year experience with 2,890 cases (including cysts) with 0.6% false suspicious later proved negative and 0% false-positive. All positives were treated by mastectomy without biopsy.

The Curie Foundation in Paris¹¹ reports 2,311 cases with 3.9% false-negative and 0.3% false-positive.

Kline and Neal¹⁰ report from Jefferson Medical College in Philadelphia a series of 150 solid breast masses aspirated.

Webb from Bristol, England,⁵ reports a 97% accuracy with 0.9% false-negative and 0.9% false-positive.

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RESULTS OF THIS STUDY

For the purpose of evaluating this procedure, we chose to divide the cases according to the *clinical* suspicion. By Review of all the records, it was determined as noted in Table 1 that 35% were performed on masses clinically considered malignant, 43% on masses clinically considered benign and the remaining 22% was undecided.

More detailed study of the clinically malignant tumors is presented in Table 2. There were no false-positive smears but there were four aspirations in three patients in which a false-negative report was rendered — all three patients proved to have carcinoma. To be noted are three patients in which aspiration correctly diagnosed carcinoma although mammograms were read as negative.

Table 3 displays the experience in 43 instances where the mass was clinically considered benign. Attention is drawn to a 31-year-old nurse with a clinically benign tumor and negative x-ray in which cytology correctly diagnosed cancer. There was one false-positive — the only false-positive in the series — which occurred in a patient with fat necrosis.

Tumors that could not be classified as either clinically suspicious or clinically benign — either due to lack of information in the record or because the physician felt undecided — are reviewed in Table 4. All smears read as either benign or malignant were correct. In two instances in each case, the mammogram report was misleading. Two aspirations reported as suspicious were both found to be from benign tumors.

COMMENT

It has been shown in medical centers throughout the world where large series of aspiration biopsies have been performed, that this is a reliable method of diagnosing most solid tumors of the breast. Hospitals reporting smaller series and short-term experience also find this to be a valuable and safe diagnostic procedure. However, it requires proper aspiration and staining technique and a cytopathologist with experience and interest in the project to make it work. This procedure yields several benefits. It may be used for rapid outpatient diagnosis — within one hour — although we have not utilized it in this manner. It is so simple and quick, and free of significant discomfort that it can be used freely. If this aspiration yields fluid, with complete disappearance of the mass, surgery is avoided and the patient can be followed safely. If the mass is solid, an aspiration biopsy can be obtained at that time to aid in diagnosis. If the smear is positive, the patient enters the hospital well prepared for definitive surgery. Today there is significant difference of opinion as to the best method of treating any particular malignant breast tumor. With "informed consent" a most important philosophy in modern medicine, some pa-

TABLE 1

ASPIRATION BIOPSY OF SOLID BREAST MASSES Maine Medical Center — 1973-1974

Clinically Malignant	—	35
Clinically Benign	—	43
Clinically Uncertain	—	22
Total		100

TABLE 2

CLINICALLY MALIGNANT TUMORS — 35

Cytology positive	19 — all malignant (3 with neg. x-rays)
Cytology negative	7 — 3 benign 4 malignant (3 pts)
Cytology suspicious	2 — all malignant (all positive x-rays)
Cytology unsatisfactory	7 — 4 malignant (2 repeat positive smears) 3 benign (1 positive x-ray)

4 aspirations in 3 pts. — false-neg.

3 aspirations gave correct dx when x-ray gave false-neg.

TABLE 3

CLINICALLY BENIGN TUMORS — 43

Cytology positive	2 — 1 malignant — neg. x-ray 1 benign — fat necrosis
Cytology negative	27 — all benign (2 positive x-rays)
Cytology unsatisfactory	14 — all benign (1 positive x-ray)

1 correct dx in face of clinical and x-ray false-neg.

1 false-positive.

TABLE 4

CLINICALLY UNCERTAIN TUMORS — 22

Cytology positive	7 — all malignant (2 neg. x-rays)
Cytology negative	11 — all benign (2 with positive x-rays)
Cytology suspicious	2 — both benign
Cytology unsatisfactory	2 — both negative

tients will want the opportunity to discuss with their physician alternate methods of therapy before they undergo anesthesia. In instances where the mass is clinically malignant and mammography and aspiration biopsy confirm this suspicion, the surgeon has the opportunity to proceed without frozen section biopsy, thus saving one-half hour of operating room and anesthesia time at a savings at this hospital of almost \$100 and avoiding a fresh incision in the field with its tumor seeding potential and requirements for double prepping, draping, etc. There are also the minor advantages of better planning of operating room time, surgeons time and arrangement for surgical assistant. This is not to say that surgeons would proceed thus in every case, but we have in several instances and centers with greater experience do it routinely.

TABLE 5

1st yr.	21 cases — one MD 1/21 false-neg. 0/21 false-pos.
2 yrs.	100 cases — 17 MD's 4 false-neg. 1 false-pos.

A smear called unsatisfactory should be considered as "no test" and repeated. Proper aspiration technique will minimize the number in this category, which means that there are not enough mammary cells in the smear to give an impression. These should not be called "negative" by the cytopathologist. A negative report should never be a reason for not doing a biopsy on a lesion that normally should be biopsied.

SUMMARY

Experience with 100 cases of small bore needle aspiration biopsy of solid breast tumors over a two-year period at Maine Medical Center has been presented. There were 4% false-negatives and 1% false-positive as noted in Table 5. There were several instances where aspiration biopsy correctly diag-

nosed tumors with misleading mammogram reports or clinical impressions.

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SOFT TISSUE SARCOMA — SOME OBSERVATIONS ON DIAGNOSIS AND TREATMENT

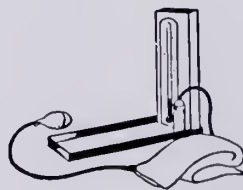
Continued from Page 93

6. A well differentiated tumor will respond more favorably with a lower incidence of metastases than a poorly differentiated tumor.
7. Early inadequate excision increases the incidence of local recurrence and reduces by approximately 50 percent the chance of cure.
8. Radiation therapy is offering an increasingly important adjunct to surgery as an alternative therapy to avoid major amputations in more distal lesions.
9. Chemotherapy at present remains ineffective in the management of primary soft tissue sarcomas in adults.

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Unorthodox Radiotherapy in Advanced Neoplasms of the Head and Neck

J. HOWARD HANNEMANN, M.D.*

Neoplasms of the head and neck account for a significant and important fraction of all tumors seen in the day-to-day practice of radiation therapy. By and large, ionizing radiation has proven most useful in the definitive management of early lesions and the palliation of advanced ones. Since the advent of supervoltage equipment, sound techniques have evolved to successfully treat a large percentage of early neoplasms. Unfortunately, satisfactory palliation of advanced tumors remains difficult and permanent local control is seldom achieved in these patients. Orthodox radiotherapy delivered at the rate of 900-1000 rads per week frequently proves incapable of coping with the massive clinical problems presented by patients with advanced malignancies of the head and neck and palliative goals often remain unachieved. Furthermore, these largely unsuccessful efforts result in the expenditure of more time and money than is consistent with the ultimate prognosis of these patients.

In hopes of overcoming one or more of the problems associated with the palliation of advanced head and neck malignancies, a treatment protocol was designed to take advantage of recent radiobiologic observations made by Elkind and others. In essence, this protocol involves the delivery of three distinct therapeutic fractions over a period of approximately nine weeks. This "8-4-4" protocol derives its name from the fact that the first fraction of treatment is administered on three consecutive days and results in the delivery of 800, 400 and 400 rads on these three successive days. Thereafter a recess of three weeks is observed and the patient is re-evaluated. If the response to the initial fraction of treatment seems to have been satisfactory, a second course of therapy ensues during which 2000 rads are delivered in daily doses of 400 rads on five consecutive days. A second three-week recess is observed before evaluating the patient for a final fraction of treatment. If undertaken, this final fraction of therapy results in the delivery of from 1600-2000 rads in four to five treatment days, again in doses of 400 rads daily. The selection of the final dose level is dependent upon the factors to be discussed below.

MATERIALS AND METHODS

Between October 1971 and April 1974, this proto-

TABLE 1

PRIMARY SITES

Tongue	12
Larynx	9
Tonsil	5
Hypopharynx	3
Nasopharynx	2
Floor of Mouth	2
Buccal Mucosa, Gingiva, Nasal Cavity, Esophagus and Mandible	1 each
Neck, Primary Site Undetermined	10 cases
Total	48 cases

TABLE 2

HISTOLOGY

Squamous Cell Carcinoma	42
Lymphoma	3
Melanoma	1
Myeloma	1
Unclassified	1

TABLE 3

EXTENT OF DISEASE (UICC)

Tumor				
T ₁	T ₂	T ₃	T ₄	T _x
0	0	13	19	16
Nodes				
N ₀	N ₁	N ₂	N ₃	
13	7	3	25	

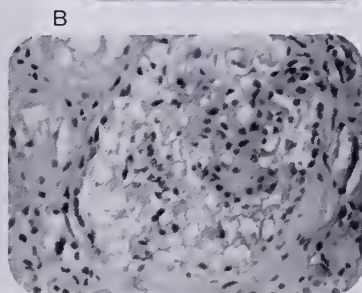
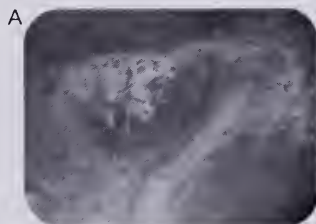
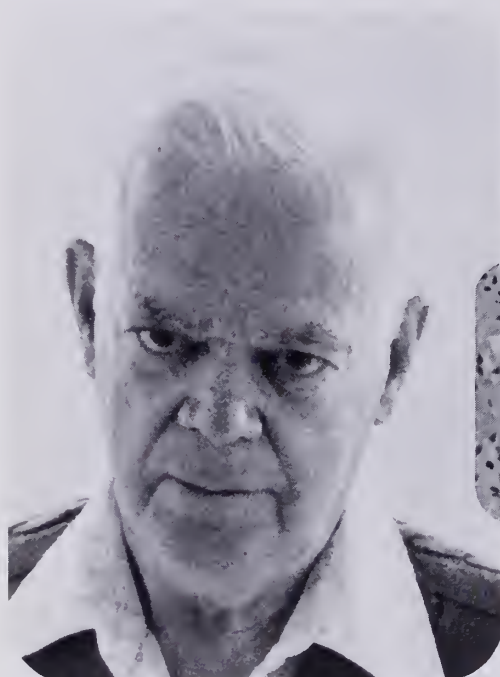
col was employed in 48 patients with advanced malignancies of the head and neck. This communication is concerned with the results of that undertaking to date. The treatment population was composed of 30 men ranging in age from 28-98 years (average 65.0 years) and 18 females with an age range from 57-93 years (average 76.2). Table 1 lists the primary tumor site which could be identified in most instances. In 10 cases, the disease presented in cervical lymph nodes without a clinically identifiable primary lesion. Histologic verification of malignancy was obtained in all cases.

The majority of these tumors were squamous cell carcinomas; however, as noted in Table 2, there were three lymphomas, one melanoma, one myeloma, and one neoplasm which at the time of diagnosis remained unclassified. At autopsy, this latter tumor proved to be a metastatic rhabdomyosarcoma of the heart.

The advanced stage of these tumors can be appreciated by study of Table 3 which outlines the extent

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What's wrong with this "patient"?*



NOTE:
a variety of typical diagnostic
signs from three patients are
combined.



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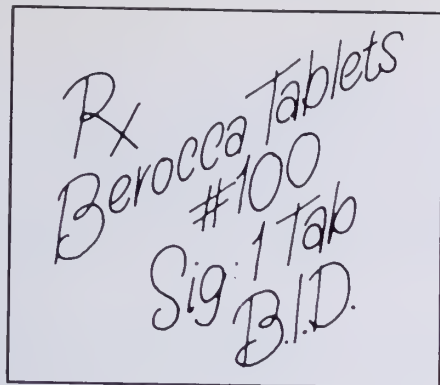
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DIAGNOSIS: Certain manifestations of diabetes mellitus are revealed in these photographs:

(A) fundus shows neovascularization and marked retinal scarring (male, age 23); (B) biopsy of kidney shows early diabetic intercapillary glomerulosclerosis (male, age 35); (C) photos 1 & 2 show edema and loss of the plantar arch (female, age 59); (D) lateral x-ray (same patient) shows dropped arch and hypertrophic and destructive changes of tarsal and metatarsal joints (Charcot's arthropathy); (E) AP confirms hypertrophic and destructive changes in (D).

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of disease according to the IUCC Classification. In all 32 instances, where the primary tumor was amenable to classification, it was placed in either category T3 (13 cases) or T4 (19 cases). The primary tumor could not be identified, had been previously excised, or was not subject to legitimate classification in the remaining 16 cases which were consequently categorized T_x. Disease in cervical lymph nodes was present in 35 cases. This disease which was usually advanced, represented the sole indication for treatment in 12 of the 16 cases whose primary neoplasms had been staged T_x. Therapy was primarily palliative in each case. Radical dose levels were selected in some instances when re-evaluation following one of more fractions of therapy suggested that a change in treatment objective would be appropriate or beneficial to the patient. As a result, a spectrum of final treatment plans was generated. In every case, therapy was initiated with the delivery of 800, 400 and 400 rads on three consecutive days.

Ten of the 48 patients received no treatment beyond the initial fraction for a variety of reasons. Four patients died during the three-week recess. Three enjoyed regression of their neoplasms during the recess but were judged to be moribund at the time of re-assessment. One elderly patient with lymphoma was deemed to have benefited sufficiently from the first fraction of therapy as to make further treatment unnecessary. One patient refused further treatment and died of her neoplasm 11 months later and one underwent successful surgical resection of what had previously been massive local disease in the neck. Thirty-eight of the 48 patients were judged to have responded satisfactorily and accordingly were treated with the second treatment fraction as previously outlined. Twenty of these 38 were withdrawn from the protocol after fraction number 2. Twelve of the 20 had persistent disease judged unlikely to be controlled by treatment fraction number 3, six responded well enough to be judged candidates for curative surgical resection, one patient was judged medically unfit for the attendant morbidity of radical radiation therapy and one patient was lost to follow up during the second recess. The remaining 18 patients received treatment fraction number 3.

All patients were treated with cobalt-60 at a source to skin distance of 70 cm. In most instances, parallel opposed portals were used although in distinctly unilateral disease (cervical adenopathy, tonsil, lateral buccal mucosa and so forth) the initial treatment fraction was frequently delivered through a single lateral portal on the side of the tumor. The treatment dose was then calculated to the most medial extent of clinical disease.

RESULTS

The response to treatment was recorded for both



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local (primary) and regional (metastatic) disease. This judgment was rendered at the time the patient either completed and responded to all three fractions of treatment or was withdrawn from the treatment protocol for the reasons previously described. The responses were scored on a scale from 0-+4. An excellent response (+4) was one which resulted in the disappearance of more than 80% of the clinically apparent neoplasm. A good result (+3) achieved 50-80% regression, a fair one (+2) resulted in a 25-50% regression and poor results (+1) realized less than 25% tumor regression. No response (0) was scored in those tumors which failed to regress or, indeed, enlarged following treatment. Responses were generally, although not exclusively, dose related. Good early responses were frequently associated with good long-term results while the converse was also true.

The response of clinical disease to treatment is outlined in Table 4. Thirty-five patients had local and/or primary disease which could be clinically assessed. Twenty-three of these enjoyed a good or excellent response to treatment (66%) and displayed regression of 50% or more of the clinically evident tumor. Sixteen of the 35 (46%) were judged to have responded in an excellent fashion with regression of more than 80% of the tumor.

Similarly, 35 patients had local and/or nodal disease which could be assessed. As anticipated, regional disease proved to be somewhat more difficult to control than did local or primary disease. Fourteen of the 35 patients or 40% enjoyed regression of 50% or more of their metastatic tumors. Ten of these 35 patients (29%) who exhibited a significant response to treatment did so in a relatively spectacular fashion with regression of over 80% of their neoplasms.

Follow-up studies are available on 47 of the 48 patients. In all cases, the elapsed time since the conclusion of radiotherapy has been at least three months, a period of time judged consistent with the determination of palliative results. Present patient status is displayed in Table 5. Twenty-two of the 48 patients have died of their disease. Nine more survive with active disease 3-12 months after the conclusion of treatment. Six of the 22 patients who are dead were among those who exhibited good or excellent responses to treatment of their local or regional disease. These six patients died without symptomatic local neoplasm and were judged to have benefited significantly from therapy. Of the nine patients who survive with active neoplasm, local or regional disease is either asymptomatic or inapparent in six, who are also judged to have benefited from treatment. Sixteen patients are presently living without clinical evidence of active disease. Thirteen of these disease-free survivors were treated with radiation therapy alone while three bene-

TABLE 4

Response to Treatment	0	+1	+2	+3	+4	Lost to F.U.
Primary Disease	2	2	7	7	16	1
Nodal Disease	6	4	11	4	10	

TABLE 5

RESULTS OF TREATMENT			
Dead			
3 mos. after R.T.		Over 3 mos.	
15		7	
Alive			
With Disease 3-12 mos. After R.T.		Without Disease	
9		16	
	3-6 mos.	Over 6 mos.	
	10	6	
Lost to Follow Up			
1			

fited from radiation therapy plus adjunctive surgery. In ten of these 16, the elapsed time since the conclusion of radiotherapy has been 3-6 months. The remaining six are clinically free of disease at intervals ranging from 6-19 months after the conclusion of treatment. Whatever the subsequent course of disease in these 16 cases, the palliative result must be considered excellent. Thus, in the overall patient population, 28 of 48 or approximately 58% responded in a good or excellent manner to palliative attempts to control local neoplasm. Although long-term results cannot yet be assessed, it is not unreasonable to believe that several of these 16 disease-free survivors will prove to have been cured by this treatment modality.

In addition to an exceptionally high response rate, other advantages of this protocol became apparent during the course of treatment. Patient morbidity was judged to be significantly less than with orthodox radiation delivered at a rate of approximately 1000 rads weekly for 5-7 weeks. During treatment with this protocol, the typical patient developed a brisk radiation mucositis 7-10 days after each treatment fraction. This mucositis remained symptomatic for 3-5 days but then subsided rapidly and was generally inapparent at the end of the three-week recess. Furthermore, compression of a radical course of radiotherapy into 13 treatment days, rather than the 30-35 days consumed during orthodox fractionation, usually results in diminished financial and domestic burdens on the patient. It allows him to utilize his most precious commodity, time, in a fashion more consonant with satisfaction than are daily trips to and from a busy cancer center.

DISCUSSION

The successful control of advanced neoplasms

requires unique radiobiologic effects which are not necessary in the treatment of less advanced lesions. Elkind has proposed a stratagem for maximizing the effect of supervoltage irradiation by changing fraction sizes and intervals and by exploiting enhanced re-oxygenation of the tumor. The treatment protocol outlined above was developed upon this stratagem.

Most large tumors and many small ones contain significant populations of hypoxic cells which are located centrally as the tumor outgrows its blood supply in peripheral expansion. The actively growing periphery or "rind" of the neoplasm can be visualized as containing most of the well-oxygenated tumor cell population. By virtue of its oxic condition, this "rind" is more sensitive than is the interior hypoxic cell population. The delivery of the initial 1600 rads of treatment is designed to maximize cell destruction while minimizing the effects of the repair of sublethal damage. Following the initial treatment fraction, the tumor "rind" as well as some of the adjacent substrata are destroyed. The three-week recess provides time for the elimination of this cellular debris and allows the underlying, previously anoxic tumor cell population to acquire a blood supply and thereby convert cells to an oxic and radiosensitive condition. Thereupon follows the second treatment fraction. It is of empiric design but with similar theoretical mechanisms. After a second rest period, a third and final fraction of treatment approaches the limits of normal tissue tolerance. These parameters of normal tissue tolerance provide the framework in which this or any similar investigational protocol must operate. The work of Ellis and Dixon has established the concept of nominal standard dose (rets) and its application of fractionated radiotherapy. Tables for the calculation of nominal standard dose as delivered in unorthodox treatment fractions have recently been published. Using these tables, we see that the present protocol results in the delivery of 1020 rets for fraction one alone and 1565 rets for fractions number 1 and 2. The total dose following fraction number 3 depends upon which of the two dosage options is employed. Early in this study the standard concluding fraction consisted of 2000 rads in five treatment days. This results in the delivery of 2057 total rets. Our two serious complications were noted in patients subjected to this treatment program.

After the availability of more sophisticated methods for computing nominal standard dose, therapy was usually concluded with a dose of 1600 rads in four treatment days. This plan results in the delivery of 1935 total rets and has been unmarked to date by serious complications or morbidity. An additional factor which seems to influence the complication and morbidity rate is the tissue volume factor. In both patients who exhibited serious post

radiation sequelae, the tissue volume included during the delivery of the entire dose of 2057 rets exceeded 1000 ccs. (10 x 10 x 10). In all those patients who tolerated the dose of 2057 rets without the development of sequelae, the tissue volume in question was substantially less than 1000 ccs.

Serious complications developed in two patients as the result of treatment. One patient with a massive carcinoma of the buccal mucosa, which also involved the adjacent gingiva, palate, floor of mouth, tonsil and tonsillar fossa, developed osteoradionecrosis of the mandible eight months after the conclusion of treatment. This complication responded symptomatically for a brief period of time to tetracycline antibiotics, but eventually required definitive management by block excision of the necrotic bone. After a prolonged surgical convalescence, the patient remains alive without evidence of disease 19 months following treatment. Another patient with a massive carcinoma of the tonsil developed a similar bony complication which was associated with local soft tissue necrosis at the tumor site. This complication developed six months after treatment and failed to respond to conservative therapeutic measures. Subsequent excision of necrotic soft tissue in and around the tonsillar fossa disclosed within the necrotic tissue many nests of viable squamous cell carcinoma.

This investigational protocol, employed until recently only in patients with far advanced malignancies, was designed to take maximum clinical advantage of theoretical and experimental radiobiologic observations. Since the inception of this investigation, more sophisticated alterations in fraction size and fractionation intervals have been suggested. While the results of the present protocol have been encouraging, it serves best as a prototype for the development of more refined and effective treatment programs which might, in the future, be employed with curative as well as palliative intent in a variety of tumor types.

SUMMARY

Forty-eight advanced neoplasms of the head and neck were subjected to radiation therapy of unorthodox fraction sizes and fractionation intervals. The overall response rate of local and regional disease was observed to be considerably higher than had been anticipated. Additional clinical studies based on recent radiobiologic observations and utilizing unorthodox treatment protocols seem warranted.

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Continued on Page 103

Carcinoembryonic Antigen

HUGH H. JOHNSTON, M.D.*

Carcinoembryonic antigen (CEA) was first characterized by Gold and associates in Montreal ten years ago. The term CEA was coined because the compound was initially found in extracts of carcinoma of the colon as well as in the intestine, liver, and pancreas of normal fetuses if taken within the first two trimesters of pregnancy. It represents another of the group of tumor antigens which now includes some cervical cancers, melanomas, sarcomas, breast tumors, nasopharyngeal tumors, hepatic tumors, and several types of chemically or virus induced tumors.

The compound is a glycoprotein with a molecular weight of 150,000 to 200,000. It migrates as a beta-globulin on immunoelectrophoresis. It resists boiling up to 40 minutes, is non-lipidic in nature, and has no enzyme activity. The compound has a protein content of 25-50%, hexose content of 25%, and contains fucose which is not present in normal colonic tissue. It presumably lacks the N-acetyl-galactosamine which is the specific blood group A marker. Its relationship to blood groups is not totally clear at this point, however.

CEA has been localized in the glycocalyx of the gastrointestinal tract. The glycocalyx is a mucoprotein on the surface of the gastrointestinal mucosal cells which exerts a protective function. When there is a breakdown of the basement membrane, the CEA enters lymphatic and vascular channels and becomes measurable in the peripheral blood.

Elevated CEA levels were initially thought to be associated primarily with carcinoma of the colon. Table 1 shows the association of elevated (greater than 2.5 ng/ml) or highly elevated (greater than 5.0 ng/ml) levels of CEA found in various malignant states. It is apparent from this table that CEA levels do not specifically denote any single type of cancer. Table 2 is a compilation of CEA levels in non-malignant disease. It is apparent from this table that CEA can be found in a host of diseases whose common denominator would seem to be the presence of inflammation. In addition to the above, CEA levels have been shown to be elevated in smokers with no evidence of malignancy. Those patients who had stopped smoking would seem to have a drop in their CEA titers (Table 3).

From the above tables, it is apparent that measurement of CEA is not specific for tumor. It is for this reason that it has not been promoted as a diagnostic aid for cancer. It can serve as a valuable ad-

TABLE 1

PERCENT OF PATIENTS WITH ELEVATED CEA LEVELS IN VARIOUS MALIGNANT DISEASES		
	CEA Titer	
	Elevated >2.5 ng/ml	Highly Elevated >5.0 ng/ml
<i>Entodermal Tumors:</i>		
Colorectal	72%	49%
Pulmonary	76	51
Gastric	61	29
Pancreatic	91	60
<i>Nonentodermal Carcinomas:</i>		
Breast	47	27
Head & Neck	51	19
<i>Noncarcinoma Malignancies:</i>		
Leukemias	25	13
Lymphoma	35	11
Sarcoma	32	5

TABLE 2

PERCENT OF PATIENTS WITH ELEVATED LEVELS OF CEA IN NONMALIGNANT DISEASE		
	CEA Titer	
	>2.5 ng/ml	>5.0 ng/ml
Emphysema	57%	20%
Alcoholic Cirrhosis	71	27
Ulcerative Colitis	31	13
Regional Ileitis	40	13
Granulomatous Colitis	48	20
Gastric Ulcer	45	16
Duodenal Ulcer	30	8
Rectal Polyps	19	4
Diverticulitis	28	7

TABLE 3

CEA LEVELS IN NONCANCER PATIENTS		
	CEA Titer	
	>2.5 ng/ml	>5.0 ng/ml
<i>Healthy Volunteers:</i>		
Nonsmokers (892)	3.0%	0%
Smokers (620)	19.0	4.0
Former smokers (235)	7.0	2.0

junct in long-range management of patients. Those individuals with histologically proven cancer that have elevated CEA levels may show a significant drop in their CEA levels subsequent to successful removal of the tumor or successful chemotherapy. It is thought that a recrudescence of tumor activity may be associated with a reappearance of elevated CEA levels. It is important not to assign this type of interpretation to samples taken within 30 days post-surgery, however. There may be a transient elevation of levels following manipulation of tumor at the time of surgical extirpation of the lesion.

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In the absence of primary pancreatic or colorectal carcinoma, titers above 20 ng/ml are generally associated with metastatic disease. It is not obligatory that metastatic lesions produce levels greater than 20, but the highest levels that have been seen have generally been associated with metastases.

When used in the proper perspective, as a management aid, CEA may broaden the diagnostic armamentarium of the clinician in following patients with known malignancies. Its primary role at the present time would seem to be that of an indicator or marker of tumor activity. Because of its association with non-malignant diseases it has no current role as a screening test for cancer. It is hoped that isolation of more specific tumor antigens such as CEA, or

isolation of more highly purified preparations of CEA itself may lead to development of a diagnostic screening test in the near future.

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*Note: Tables modified from reference 1.

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Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The bylaws of the Maine Medical Association were amended in June of 1973 as follows: Chapter I, Section 11, — "Each member of the Maine Medical Association shall be required to report his activities in continuing medical education every year according to a format provided by the Committee on Continuing Medical Education."

Please fill in your activity report promptly and return to the M.M.A. office, P.O. Box 250, Brunswick, Maine 04011.

Observations on the Clinical and Pathologic Features of Myelofibrosis

LOUIS G. BOVE, M.D.* and JOSEPH P. FANNING, M.D.**

Myelofibrosis is a descriptive term of a specific pathologic process, a process which is now easily witnessed through the technique of percutaneous bone marrow biopsy. Myelofibrosis is often referred to as primary, or idiopathic myelofibrosis, or secondary. It may be secondary to drug toxicity, i.e., benzene, arsenic, or irradiation; to a chronic infection, i.e., tuberculosis; or to metastatic disease, i.e., breast, prostate, lung or stomach. Our observations were made on primary or idiopathic myelofibrosis, which is most often associated with myeloid metaplasia, a state of extramedullary hematopoiesis and leukoerythroblastosis. There are many names and terms referring to similar states, these terms usually reflecting that aspect of the disease state which impressed the author.¹ We favor the term idiopathic myelofibrosis or myeloid metaplasia, myelofibrosis (MMM). It must be stressed that the myeloid metaplasia is not a result of, or dependent on, the myelofibrosis or vice versa — each being a distinct entity in themselves. Both are a manifestation of a stimulus to the primitive multi-potential mesenchymal cells. The classification of idiopathic myelofibrosis would therefore seem to be best described as belonging to the spectrum of myeloproliferative disorders, a term originally coined by Dr. Dameshek.² This term has not been accepted by all because of the associated concept of transitions within this spectrum from one disease state to another.³ Our small experience favors the former concept of a myeloproliferative disorder, although we accept the fact as further knowledge becomes available regarding the pathogenesis of these states that we may be able to be more specific regarding disorders of the hematopoietic tissue and the term myeloproliferative would be inappropriate.

We have been impressed with the frequency of this syndrome, especially when compared with other more well-known myeloproliferative disorders in a general hospital such as the Maine Medical Center (basically still a community hospital, although currently about ¼ of the patients are referred from outside the Greater Portland area). In the 18 month period from January of 1973 through June of

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TABLE 1

IDIOPATHIC MYELOFIBROSIS SYMPTOMS AND PHYSICAL FINDINGS (14 CASES)	
WEAKNESS, FATIGUE, ETC.	13
WEIGHT LOSS	6
PALLOR	8
ABDOMINAL MASS	8
BLEEDING MANIFESTATIONS	4
SPLENOMEGALY	13
HEPATOMEGALY	7
PALLOR	10
PETECHIAE OR ECCHYMOSES	4
SKIN RASH	3
LYMPHADENOPATHY	1

TABLE 2

IDIOPATHIC MYELOFIBROSIS LABORATORY FINDINGS (14 CASES)	
ANEMIA	12
RBC MORPHOLOGY	
POIKILOCYTOSIS WITH TEAR-DROP FORMS	12
NUCLEATED RBC'S	12
WBC (X 10 ³)	
LEUKOPENIA <4.8	5
NORMAL	2
LEUKOCYTOSIS > 10.8	7
DIFFERENTIAL COUNTS	
IMMATURITY (LEFT SHIFT, i.e., MYELOCYTES)	12
BLAST CELLS	9
BASOPHILIA > 1%	4
PLATELET COUNTS	
THROMBOCYTOPENIA < 150,000	7
NORMAL	3
THROMBOCYTOSIS > 350,000	4
MORPHOLOGY — GIANT PLATELETS	10
LEUKOCYTE ALKALINE PHOSPHATASE (10 STUDIES DONE)	
ELEVATED	9
NORMAL	1

1974 there have been 14 new cases of idiopathic myelofibrosis, while only 5 new cases of polycythemia vera and 8 new cases of chronic myelogenous leukemia in the same period. There were 6 cases of myeloproliferative disorders, type unspecified. For reference there were 18 new cases of acute myelogenous leukemia. For contrast there were 19 cases of pulmonary tuberculosis, 16 cases of carcinoma of the pancreas and 14 cases of sub-acute bacterial endocarditis in the same period, which attests to the frequency of this syndrome as a "not uncommon" medical diagnosis.

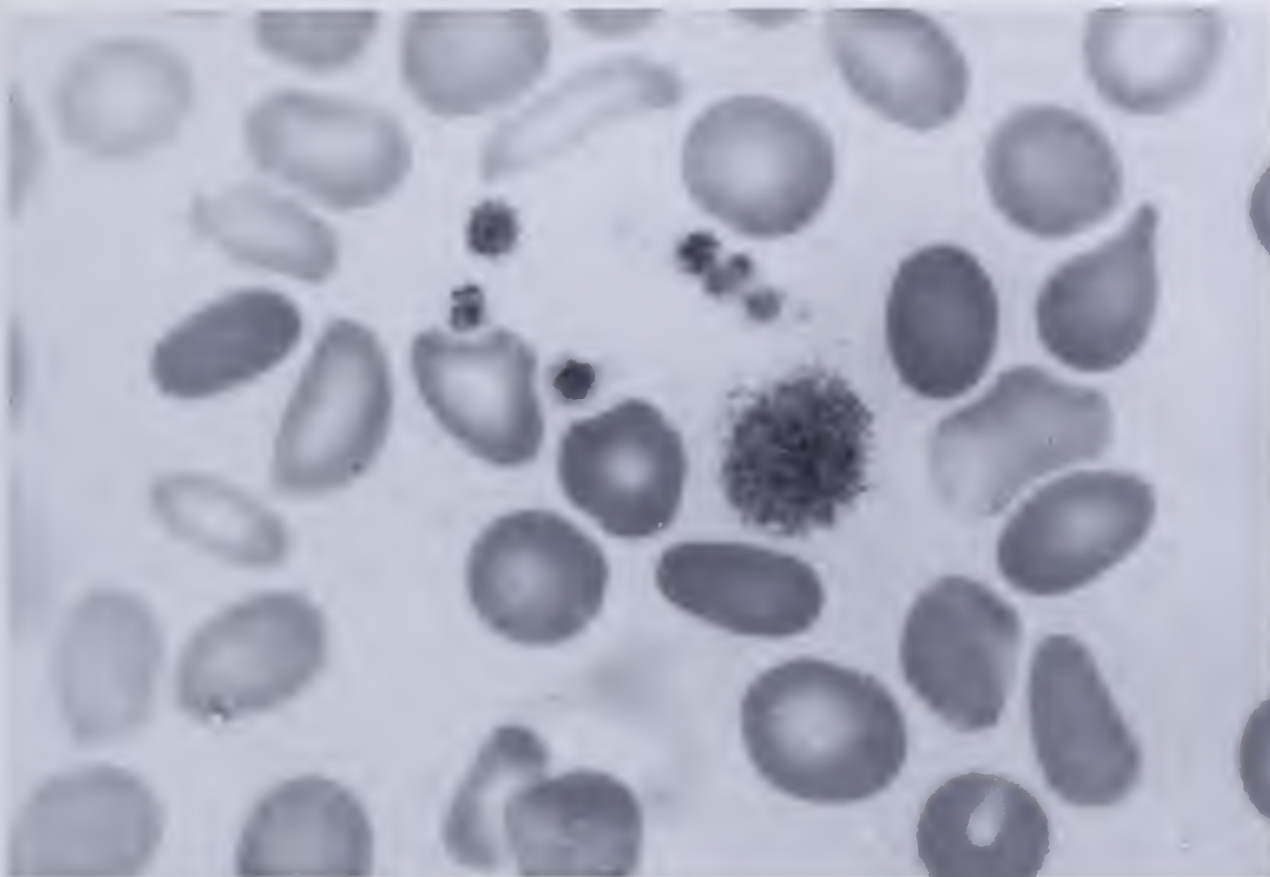


Fig. 1. Smear of peripheral blood showing considerable variation in shape of red blood cells, with several tear drop forms. A giant platelet is present in the center of the field. (Wright-Giemsa Stain X3200)

PRESENTING SYMPTOMS AND PHYSICAL FINDINGS

The presenting symptoms of our patients with idiopathic myelofibrosis are outlined in Table 1. Symptoms often reflect the duration of the disease. Some patients may be asymptomatic, the diagnosis being suggested after a routine history and physical examination. In our small experience, only two patients fell into the latter group, while all the others were symptomatic when first seen with complaints of weakness, fatigue, weight loss, pallor or an abdominal mass. Two patients presented with ruptured spleens.

On examination all of the patients except those two who presented with ruptured spleens appeared well, and not necessarily chronically ill. The leading physical finding was, as it is in most large series,^{3,4,5} gross splenomegaly. Only one patient did not present with splenomegaly. The spleen is often markedly enlarged, and this gross splenomegaly in an apparently well patient is the most significant diagnostic clue in the routine physical exam. Other findings on physical exam are listed in Table 1. Although hepatomegaly was present in half of our patients, the liver enlargement was not of the degree of en-

largement as that of the spleen. Hepatomegaly would be unusual without splenomegaly, again stressing the importance of the enlarged spleen.

LABORATORY FINDINGS

Like the splenomegaly on physical exam, the peripheral blood findings, specifically the leukoerythroblastosis, is the second outstanding feature of this syndrome. The laboratory findings are outlined on Table 2. All but two patients had anemia, and in half of these it was severe, with hemoglobin values of less than 8 gms. By history several of these patients had been described by their referring physicians as having a "refractory type of anemia," referring to treatment. The red cell morphology is classic and we refer to the marked poikilocytosis with tear-drop forms (Figure 1). These tear-drop forms were present in *all* but two cases. Nucleated RBC's were also frequent and present in twelve cases, the numbers of the latter being increased markedly after splenectomy. The leukocyte count varies, with over half of our patients presenting with leukocytosis, but of equal importance is the large number who presented with leukopenia, a fact that is not always appreciated. The leukocytosis was not

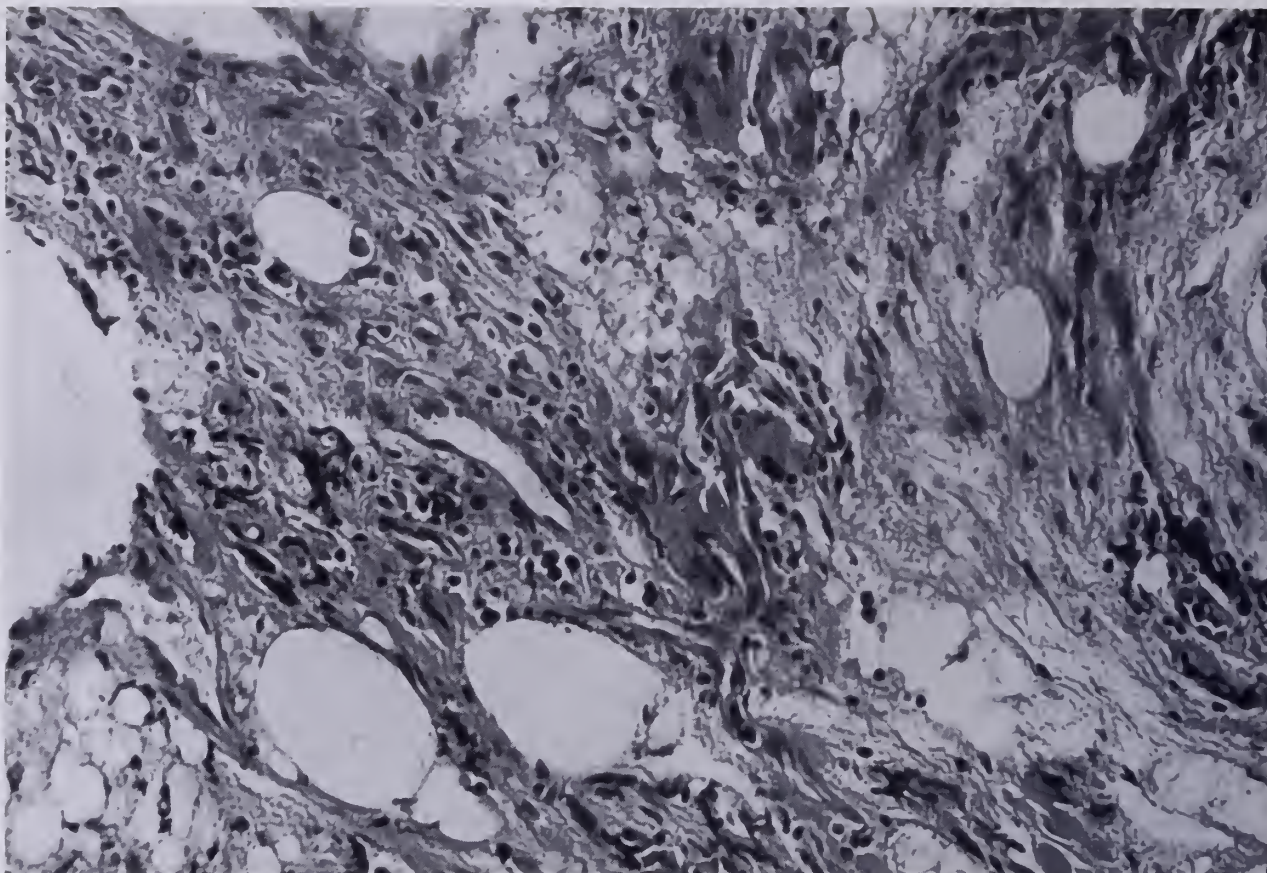


Fig. 2. Bone marrow showing considerable replacement by connective tissue, with remaining clusters of megakaryocytes and scattered erythroid cells. (H&E Stain X600)

as excessive as that often seen in chronic myelogenous leukemia (CML), our highest count being only 48,000. The granulocyte immaturity is well reported with myelocytes, metamyelocytes, and blasts being present in the smear. Nine of our cases showed blasts, the number of blasts being quite variable, but in a third of these there were over 5% blasts, a finding once reserved for acute leukemia. Basophils are also often noted. Thrombocytopenia appeared to be more common than thrombocytosis, and abnormal platelet morphology with giant platelets was present in ten cases. We did not observe megakaryocyte fragments, which are often described. Platelet function was not studied.

The finding of an elevated leukocyte alkaline phosphatase (LAP) is well described, and most helpful in distinguishing this entity from CML. Ten of our patients were studied, and in all but one was the LAP score increased. Cytogenic studies were not regularly done, and no comment is made other than the fact that the Philadelphia chromosome was not present in the four cases studied. This marker seems generally specific for CML. Vitamin B₁₂ levels were not done in numbers to be significant, but the levels were elevated in half of those studied,

although the levels were not in the range seen in untreated CML.

BONE MARROW FINDINGS

The third classic feature of this syndrome is the fibrosis within the bone marrow cavity. Thirteen of fourteen marrow aspirations were so-called "dry taps," and one aspiration showed a hypercellular marrow.

In 12 of the 14 cases bone suitable for evaluation was obtained by posterior iliac crest biopsy. Seven of the twelve bone marrow biopsies showed fibrosis and hypocellularity (Figure 2). Five of the twelve showed marked hypercellularity.

In the cases showing fibrosis, little erythropoiesis or granulopoiesis was evident. The marrow spaces were extensively replaced by loose connective tissue comprising fibroblasts, collagen, and reticulum fibers and containing scattered plasma cells and reticulum cells. More often than not reticulum fibers were more conspicuous than collagen fibers (Figure 3). In all of these cases, however, considerable numbers of megakaryocytes remained and showed a distinct tendency towards clustering and pleomorphism. All of the cases showed a mild to mod-

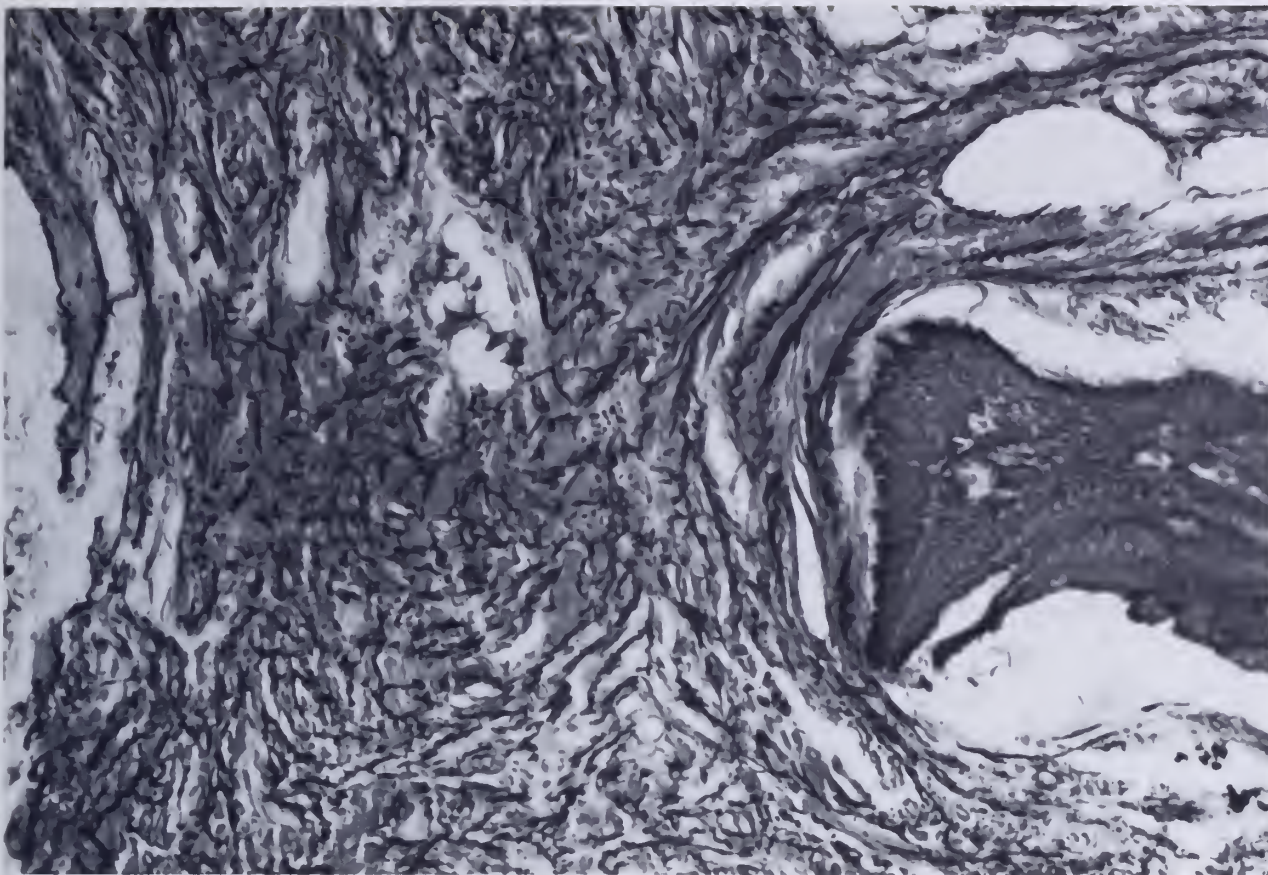


Fig. 3. Bone marrow showing diffuse increase in reticulum fibers and focal thickening of bone trabeculae. Reticulum fibers are coarse and show a tendency to attachment to bone edges. (Snooks Reticulum Stain X600)

erate degree of osteosclerosis, the degree generally correlating with the extent of fibrosis. The bone thickening seemed to be due to apposition of membrane formed bone to existing bone trabeculae and in some instances spicules of membranous bone could be seen in areas of fibrosis away from pre-existing bone trabeculae.

In all five cases showing hypercellularity, marrow fat was reduced to less than 10% of total marrow present. While the hypercellularity affected all cell series, erythroid cells and megakaryocytes predominated. The megakaryocytes, as in the cases showing fibrosis, were particularly conspicuous and showed a tendency towards clustering and pleomorphism. A diffuse increase in reticulum fibers was demonstrated in all of these cases. We felt that certain characteristics of the reticulum pattern, distinct from the non-specific diffuse increase seen in other states of hypercellular bone marrow, permitted us to strongly suspect, at least, the presence of myeloid metaplasia/myelofibrosis. These consisted of a coarsening and strand-like arrangement of reticulum fibers with appositional attachment to bone trabeculae and passage at times into their tips (Figure 3).

In five of the cases with bone marrow biopsies, tissue from spleen and/or liver were available for study. Myeloid metaplasia of varying degree was present in all cases. There was no apparent correlation between the degree of myeloid metaplasia and the morphological appearance of the bone marrow.

FOLLOW-UP AND OUTCOME

Some authors have commented on the increased mortality and morbidity of patients with idiopathic myelofibrosis associated with surgery.⁴ Nine of our fourteen cases had major surgical procedures, including five splenectomies, an open-heart, hip replacement, etc.; and there were no deaths, but there was an increase in bleeding problems postoperatively. Only one of our patients had a documented myeloproliferative disorder prior to this diagnosis of idiopathic myelofibrosis. This was a case of polycythemia vera.

There have been eight deaths and six survivals within the short period of follow-up, which I think suggests an advanced stage of the disease when first seen by us.

Of the 12 cases studied by bone marrow biopsy, five died and four were autopsied, allowing for pos-

sible documentation of progressive changes in tissue patterns. Such pattern changes did not, however, emerge.

DISCUSSION AND CONCLUSIONS

Although our series is small in comparison to others, namely, Silverstein,⁵ Rosenthal and Maloney,⁶ Glasser and Walker,³ we are impressed with the frequency of this syndrome in a community oriented hospital when compared to other more well known myeloproliferative disorders. We stress again the triad of splenomegaly, leukoerythroblastosis, and myelofibrosis on marrow biopsy. Our laboratory findings are quite consistent with other large series, except for the lack of x-ray findings of osteosclerosis.

The variable pattern of the bone marrow in myeloid metaplasia/myelofibrosis is well recognized.^{1,4} The degree of cellularity varies not only from one patient to another, but also in different skeletal sites in the same patient and even, at times, in different places in the same bone marrow specimen used for evaluation. In this small series, the incidence of 40% of cases showing initial bone marrow hypercellularity correlates with the incidence noted in much larger studies.^{1,4,5} No significant correlation between the morphologic appearance of the bone marrow and the extent of extramedullary hematopoiesis was noted. The pattern and distribution of extramedullary hematopoiesis was similar to that described in other studies — recapitulating the pattern of embryonic blood formation.^{1,4} Despite the low incidence of radiologically diagnosable osteosclerosis in our cases, a reasonable correlation was noted between the degree of microscopic osteosclerosis and the extent of myelofibrosis. Osteosclerosis also appeared to be due to membranous bone formation in areas of fibrosis. We cannot reliably comment on any change of pattern of bone marrow morphology with respect to progression from a hypercellular state to a fibrotic state, but we do wish to note that in one case with extensive myelofibrosis in the bone marrow biopsy the autopsy disclosed a pan-hyperplastic marrow with accompanying extensive myeloid metaplasia. We realize of course that in an instance such as this we are comparing morphological patterns from different skeletal sites.

We have not as yet seen the incidence of leukemia described in other reports.^{7,8} Two cases did

die of an associated malignancy related to the presence of myelofibrosis, pointing to the inherent malignant potential of this disorder. However, neither case could be described as typical or usual for idiopathic myelofibrosis. One was a case of polycythemia vera progressing through myelofibrosis to acute myelomonocytic leukemia and the other was a most unusual case of childhood myelofibrosis, which terminated in a bizarre type of malignancy involving immature myeloid tissue.

Although we recognize that there is no specific therapy, a comment is in order. Therapy may well be meddlesome and may contribute to an increase in both morbidity and mortality in what basically is a rather long smouldering and initially benign disease. The indications of splenectomy are clearcut, i.e., progressive hypersplenism, or symptoms secondary to the massive size of the spleen, or rupture of this organ, but timing is important as once the spleen is removed, massive hepatomegaly follows. The moderate leukocytosis seen in idiopathic myelofibrosis is not of harm to the patient and the premature and excessive use of alkylating agents only adds to the risk of infection.

Radiotherapy has been helpful when a patient's poor risk negates surgical removal of an enlarged spleen and was successful in decreasing splenic size and lessening symptoms in several cases. X-ray to an enlarged liver once the spleen has been removed must be done with extreme care, as this is the main source of hematopoiesis, and severe pancytopenia with the inherent risks of infection and hemorrhage develop.

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- Daniel Hamaty, M.D. of Guilford, Connecticut
- David R. Boyd, M.D. of West Hyattsville, Maryland
- Edward Campbell of Toronto
- John F. Hinds of Toronto

SPECIALTY GROUP SPEAKERS —

- Arthur A. Sasahara, M.D. of West Roxbury
- Howard M. Kern, M.D. of Washington
- Robert M. Knowles, M.D. of Portland

EVENTS OF INTEREST —

Saturday, June 14

2:00 P.M. First Meeting of the House of Delegates

Presentation of the A. H. Robins' Physician Award for Community Service

Presentation of the Maine Blue Cross and Blue Shield "Award of Appreciation"

Sunday, June 15

A.M. Reference Committee Meetings

2:00 P.M. Second Meeting of the House of Delegates

Election of President-elect and Executive Committee District Members

SUNDAY EVENING — LOBSTER DINNER

MONDAY EVENING — ANNUAL BANQUET

Pharmacology and Clinical Use of Antacids

F. WILLIAM GREEN, JR., M.D., RICHARD A. NORTON, M.D. and
MARSHALL M. KAPLAN, M.D.

ABSTRACT

Liquid antacid suspension should be given at least as often as one hour after each meal and at bedtime. In the treatment of the acute phase of acid-peptic disease, hourly antacid is recommended. The dose should be planned in terms of milliequivalents of acid neutralizing capacity and should be adjusted according to the type of disease under treatment.

All antacids have side effects, the most serious of which are metabolic. In clinical terms, the harmful systemic side effects of calcium carbonate and sodium bicarbonate outweigh their benefit as neutralizing agents; they should rarely be employed in the treatment of acid-peptic disease. The more common antacid side effects of diarrhea and constipation are best managed by appropriately alternating the agents or by using one of the various antacid mixtures.

Antacids represent a widely accepted mode of treatment for acid-peptic disease. They are also taken for the relief of other complaints of gastrointestinal origin. In the United States, physician and patient acceptance is so great that more than \$120 million are spent annually on such preparations despite uncertainty as to their overall clinical benefit. Rapid relief of typical ulcer pain is a common observation, but there are conflicting reports as to the beneficial effect of antacid therapy in promoting healing or decreasing complications in acid-peptic disease.^{1,2} This article will discuss antacid pharmacology with particular reference to the clinical use

"It once happened that all the other members of a man mutinied against the stomach, which they accused as the only idle, uncontributing part in the whole body, while the rest were put to hardships and the expense of much labour to supply and minister to its appetites."

From Plutarch's Lives, Alcibiades.

of these agents in treating acid-peptic disease.

The presence of both acid and pepsin is considered essential in the genesis of peptic ulcer disease. In theory, antacid therapy may be of benefit for two reasons. First, in reducing total acid load, less hydrogen ion is available for back-diffusion through the gastric mucosa and less acid is delivered to the duodenum for chemical neutralization and the concomitant inactivation of pepsin there. Second, raising the intragastric pH takes pepsin above its optimum proteolytic activity range of 1.5-2.5 pH.³⁻⁵ Above pH 4.0 peptic activity is virtually absent. A few antacids may exert an antipepsin effect independent of pH change: aluminum hydroxide by adsorption of pepsin⁶ and calcium carbonate by some unknown mechanism.⁴ The clinical importance of these non-pH related antipepsin effects is at present unknown. The significance of the astringent and demulcent properties of antacids is also unclear.

ACTION OF ANTACIDS

Commonly used antacids are non-absorbable salts which are poorly water-soluble at neutral pH. However, in acid media these salts are solubilized and release anions which are then available to combine with or neutralize hydrogen ions. In this way, gastric acid *proportionately* generates reactive base thus avoiding base overload. Some antacids, such as magnesium hydroxide and sodium bicarbonate, are quickly solubilized at gastric pH and provide rapid, full buffering effect. Others, such as aluminum hydroxide and calcium carbonate are slowly solubilized and develop significant reactivity over ten to thirty minutes.⁷ Since only solubilized antacid has the capacity to react with hydrogen ions, the dissolution rate or ease of solubility of an antacid preparation is an important determinant of its ultimate

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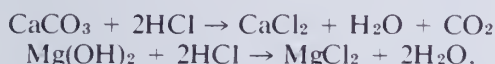
Drug Therapy Reviews is supported by a grant from the Bingham Associates Fund through a grant-in-aid to the "Focus on Pharmacy" program, a joint project of the Departments of Pharmacy of the Maine Medical Center, Portland, and the New England Medical Center Hospital, Boston.

Address reprint requests to Dr. Green, Gastroenterology Service, New England Medical Center Hospital, Boston 02111.

neutralizing capacity.⁸ This in turn, is influenced by the nature of the formulation, i.e., whether it is a suspension, powder, or tablet. Suspensions are more easily solubilized than powders or tablets and therefore have greater neutralizing effect. Aluminum hydroxide gel loses most or all of its neutralizing potency in the process of drying to a tablet or powder form.⁹

The gastric pH value at which adequate solubilization takes place is determined by the physicochemical properties of a given antacid or antacid mixture. The physicochemical properties of aluminum hydroxide, for example, are such that it cannot elevate intragastric pH above 4. In fact, within the limits of tolerable and safe doses, most antacids do not raise and hold gastric pH above 4 or 5. Hence, the terms "neutralization" and "neutralizing capacity" are used to refer to a significant reduction in gastric acidity, not to the elevation of pH to 7 or the attainment of chemical neutrality. A pH change of three units from 1.2 to 4.2, for example, represents a one thousand-fold reduction in hydrogen ion concentration.

In the stomach, antacid may exist in two forms: dissolved (reactive), and undissolved (unreactive). The undissolved, excess fraction is passed from the stomach at a somewhat slower rate than the dissolved⁷ and remains relatively unchanged and unabsorbed throughout the gastrointestinal tract. Dissolved (solubilized) antacid reacts with gastric hydrochloric acid according to a simple equation. Examples are:



Chloride salts formed in the process of neutralization of gastric acid are absorbable, but these are largely converted to nonabsorbable substances at intestinal pH and their absorption is thereby limited. Nevertheless, some cation does escape early duodenal conversion to nonabsorbable salts and is absorbed.

Sodium bicarbonate is an exception to the above explanation. It is a highly soluble, absorbable substance which, from the standpoint of an antacid, has none of the safeguards of compounds such as magnesium hydroxide, aluminum hydroxide or even calcium carbonate. Sodium bicarbonate neither develops neutralizing effect proportionate to gastric acidity, nor is its absorption fixed or limited.

SIDE EFFECTS AND COMPLICATIONS

In view of the relatively large doses of antacids used in the treatment of gastrointestinal complaints, it is not surprising that side effects are common. Fortunately, these are rarely serious. The most frequent are those produced directly on the gastrointestinal tract itself.

The osmotic effect of soluble but poorly absorbed salts of magnesium probably causes the diarrhea which frequently accompanies magnesium hydroxide therapy.⁷ Conversely, the precipitation of insoluble calcium and aluminum salts may explain the constipation noted when calcium carbonate or aluminum hydroxide antacids are employed.⁷ Diarrhea produced by magnesium hydroxide may occasionally be severe and lead to metabolic complications. Aluminum hydroxide antacid therapy has been implicated in several reported cases of ileal and colonic obstruction.¹⁰ Proprietary mixtures have been developed to avoid the common intestinal side effects.

Serious systemic side effects occur to the extent that absorbed antacid cation or anion is able to alter the internal milieu. The magnitude of such an alteration depends not only on the quantity of the offending ion absorbed but also on the adequacy of appropriate organ systems to compensate for its excessive absorption and systemic presence. Thus, the excess bicarbonate absorbed after ingestion of two to four teaspoonfuls of sodium bicarbonate is compensated by increased renal excretion while, at larger doses, excretory capacity may be exceeded and serious alkalosis can result. In patients with renal insufficiency, magnesium-containing antacids will produce hypermagnesemia due to decreased renal clearance of this cation.

Absorption of small amounts of sodium existing as contaminants in most antacids can result in further fluid retention in patients with congestive heart failure, cirrhosis, or nephrosis.¹¹ The detrimental effect of sodium bicarbonate administered to such patients is obvious.

The absorption of calcium derived from calcium carbonate antacids, although limited, is significant and may affect both serum calcium level and acid-base balance. Approximately 10% of the reacted portion of an administered dose of calcium carbonate escapes chemical reconversion by duodenal bicarbonate to calcium carbonate or to other unabsorbable calcium-containing compounds.⁷ This fraction is available for absorption and may lead to elevated serum calcium levels.^{2,12,13} To the extent that calcium is unavailable to react with intestinal bicarbonate, either because of previous absorption or by combination with other anionic groups in the gut, a bicarbonate load is added to the system and alkalosis may result. Normal renal excretory function will usually compensate for this tendency toward metabolic alkalosis. However, in patients with high acid secretory rates who are taking large doses of calcium carbonate, enough soluble calcium chloride may be formed and absorbed to produce the so-called milk-alkali syndrome in the absence of either milk or bicarbonate ingestion.¹⁴ This syndrome is characterized by hypercalcemia, metabolic

alkalosis, and occasionally renal insufficiency. Possible presenting complaints include anorexia, constipation, change in mental status, and other manifestations of hypercalcemia.

Calcium carbonate is the only antacid shown to produce the reflex hypersecretory state called "acid rebound."¹² This is probably a direct effect of calcium on the gut mucosa and not secondary to actual calcium absorption.¹² Whether or not the excellent neutralizing capacity of calcium carbonate is adequate to compensate for this induced excess acid secretion is unknown.

Antacids can impair the absorption of certain drugs and dietary substances. The absorption of ferrous sulfate is decreased by coadministration of magnesium trisilicate¹⁵ or sodium bicarbonate.¹⁶ Absorption of chlortetracycline,¹⁷ chlorpromazine,¹⁸ isoniazid,¹⁹ and digoxin²⁰ can be delayed or reduced when given together with antacids. Whether concomitant administration of antacid reduces the absorption of corticosteroids is at present unknown.

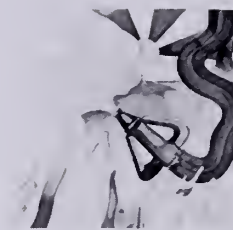
A phosphorus depletion syndrome has recently been recognized in patients on chronic aluminum hydroxide therapy who, in addition, have either low dietary phosphorus intake or excessive losses from malabsorption.²¹ Phosphorus balance is further disturbed by fecal loss of phosphorus as aluminum phosphate. The clinical presentation is that of anorexia, weakness, and malaise. Severe skeletal disease may ensue due to calcium and phosphorus resorption. The phosphate-depleting property of aluminum hydroxide is often used for therapeutic purposes in patients with hyperphosphatemia due to renal failure.

ANTACID MIXTURES

Antacid mixtures containing magnesium hydroxide and a constipating antacid, such as aluminum hydroxide, have been developed to minimize the cathartic effect of magnesium hydroxide but still retain its excellent acid neutralizing effects. Although bowel function side effects may be offsetting in the compounding of these mixtures, other side effects or complications, such as hypermagnesemia, phosphorus depletion, and water retention, are not.

The total neutralizing capacity of a mixture appears to be roughly equivalent to the sum of the capacities of its constituents, though the pH value at which buffering occurs may be altered. Thus, 8 ml (600 mg) of magnesium hydroxide will hold 20 mEq of hydrochloric acid at a pH above 8, whereas the combination of 8 ml (600 mg) of magnesium hydroxide and 8 ml (600 mg) of aluminum hydroxide gel buffers only 5 mEq hydrochloric acid above pH 8, but thereafter is able to buffer an additional 25 mEq

Continued on Page 113



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Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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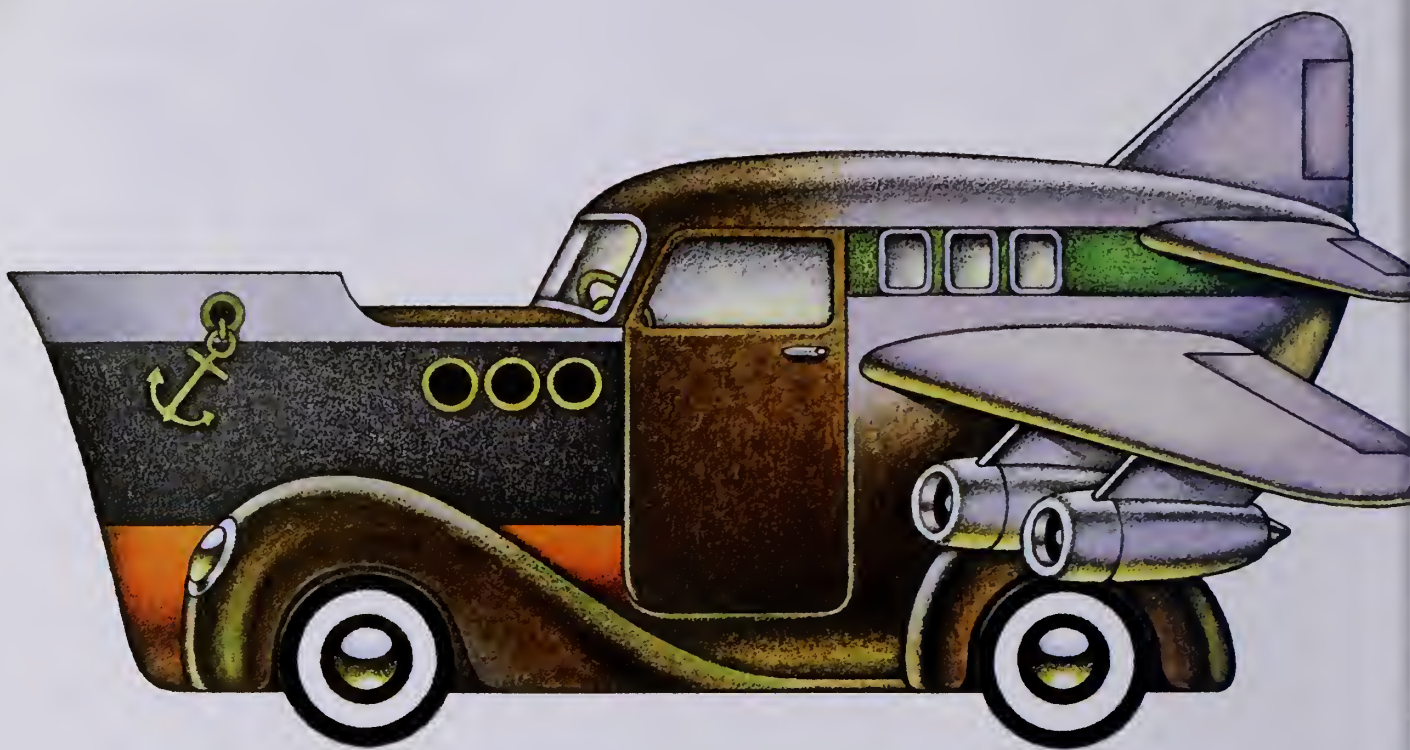
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at about pH 4.⁹ If the goal of therapy is to hold the intragastric pH in the range of 6 to 8, then the inclusion of aluminum hydroxide in the mixture is detrimental.

ANTACID THERAPY

Choice of an antacid regimen in clinical practice depends upon the acid secretory rate of the stomach, gastric emptying time and the neutralizing capacity of the proposed antacid.

Patients with duodenal ulcer disease usually have higher acid outputs than persons without duodenal ulcers. This does not appear to be true for gastric ulcer patients. In addition, duodenal ulcer patients have an exaggerated acid output response to a meal stimulus.²⁴ Acid output is always highest in the early post-prandial period. However, meal contents provide significant buffering capacity such that *measured* acidity will not become high until one and a half to two hours after the meal.⁴ With elimination of the meal buffer from the stomach, measured acidity becomes elevated and is generally highest for the hour or two before the next meal. Nocturnal acidity is greatest between 11:00 p.m. and 2:00 a.m. and exceeds the high levels found preprandially. It is precisely during these unbuffered periods that typical ulcer pain arises and that additional buffer is required.

The factor of gastric emptying accounts for the discrepancy between in vitro neutralizing capacity and the observed in vivo neutralizing effect of antacids. Antacid equivalents several times the actual interim hydrochloric acid output must be administered to maintain reduced gastric acidity for even an hour.^{22,23} In contrast to the brief twenty to sixty minute effect of antacids administered in the fasting state, antacids taken one hour after meals have a neutralizing effect which lasts two to three hours.^{4,23} This is because the rate of gastric emptying is reduced postprandially. Duodenal ulcer patients empty their meal buffer at a rate about twice that of normal controls.²⁴ Thus, in addition to greater acid output and exaggerated acid output response to a meal stimulus, the duodenal ulcer patient has a shorter gastric emptying time.

There is considerable variation in the in vitro neutralizing capacity of the commonly used antacids.^{4,8,23,25} A good *relative* correlation between in vitro neutralizing capacity and in vivo neutralizing effect has been demonstrated.²³ Thus, knowing the approximate acid output and gastric emptying time of a given patient, it becomes possible to estimate the dose of a particular antacid needed to provide significant acid reduction for a given time period. For purposes of standardization, antacid doses should be thought of in terms of their quantitative neutralizing value in "milliequivalents of antacid."^{22,23}

GUIDELINES FOR ANTACID THERAPY

Antacid therapy should be individualized. Patient compliance will be maximized if the preparation is palatable, prescribed in tolerable doses on an acceptable schedule, and is relatively free of bothersome side effects. The presence of renal insufficiency, malabsorption or congestive heart failure or the simultaneous administration of other medications should be taken into consideration before selecting a particular antacid or designing a therapeutic regimen. Antacid potency determines the actual dose required. Cost to the patient is another important factor and may vary as much as tenfold per equivalent neutralizing dose (see Table 1). The physician should suggest several appropriate antacids and allow the patient to select the one(s) best tolerated from the standpoint of palatability and change in bowel habits.

SELECTION OF AN ANTACID

Sodium bicarbonate and calcium carbonate antacids, while extremely effective as neutralizing agents, are not recommended in the treatment of acid-peptic disease.^{9,23} Small, infrequent doses of sodium bicarbonate may be appropriate for the relief of occasional "heartburn" and "gastric upset," but many physicians never use sodium bicarbonate.

Magnesium hydroxide is the safest and most potent substitute for calcium carbonate or sodium bicarbonate. In the absence of renal failure, it should be one of the antacids selected for most patients with acid-peptic disease. Magnesium hydroxide is best prescribed in combination with a constipating agent such as aluminum hydroxide gel, either concurrently in a proprietary mixture, or alone in an alternating dosage regimen. Aluminum hydroxide gel alone and mixtures containing magnesium trisilicate are also used. However, these preparations are less potent neutralizing agents. In general, a suspension is preferable to the same antacid in powder or tablet form.

CLINICAL APPLICATION

The administration of antacids one hour after meals and at bedtime is imperative. These are the times when antacid retention will be greatest and when unbuffered acidity is rising towards maximal. The routine administration of antacids with, shortly before, or shortly after meals is inconsistent with the above principles and is not recommended.

While buffering effect of an antacid given one hour after a meal may still be present three hours post-cibum,⁴ Fordtran recommends follow-up antacids at hourly intervals in the therapy of acute duodenal and gastric ulcers. This intensive hourly ant-

*Milliequivalents of antacid is defined by the mEq of hydrochloric acid required to keep an antacid suspension at pH 3.0 for two hours in vitro.²³

TABLE 1

CHARACTERISTICS OF ANTACIDS				
<i>Antacid (Suspensions)</i>	<i>Components^a</i>	<i>Neutralizing Capacity^b (mEq/15 ml)</i>	<i>Cost per 40 mEq (\$)</i>	<i>Comments, Side Effects, Special Uses</i>
<i>Single-entity</i>				
Magnesium hydroxide (Milk of Magnesia)	———	35	.05	Diarrhea limits patient acceptance; produces hypermagnesemia in patients with renal insufficiency.
Aluminum hydroxide (Amphojel)	———	29	.11	Constipation; phosphorus depletion; combats hypermagnesemia of renal failure.
Calcium carbonate (Titrilac ^d)	———	58	.08	Produces "acid rebound;" milk alkali syndrome occasionally results.
Sodium bicarbonate	———	———	———	Metabolic alkalosis; exacerbates water retention.
Dihydroxyaluminum aminoacetate (Robalate)	———	17	.28	
Aluminum phosphate (Phosphaljel)	———	6	.59	
Magaldrate ^e (Riopan)	———	33	.09	Low sodium content; good in fluid retention states.
<i>Mixtures containing aluminum hydroxide and magnesium hydroxide</i>				
Aludrox	1, 2	42	.08	
Creamalin	1, 2	39	.07	
Di-Gel	1, 2, 3	37	.14	Aluminum hydroxide-magnesium hydroxide mixtures may produce diarrhea, phosphorus depletion, hypermagnesemia (in renal insufficiency) and increased fluid retention.
Gelusil-M	1, 2, 4	34	.10	
Maalox	1, 2	39	.08	
Mylanta	1, 2, 3	36	.09	
Mylanta II	1, 2, 3	62	.08	
Win-gel	1, 2	34	.09	
<i>Other Mixtures</i>				
Camalox	1, 2, 5	54	.06	Calcium-containing (see above).
Ducon	1, 2, 5	105	.04	Calcium-containing (see above).
Gelusil	1, 4	20	.16	Silicate kidney stones reported.

^a 1-aluminum hydroxide, 2-magnesium hydroxide, 3-simethicone, 4-magnesium trisilicate, 5-calcium carbonate.

^b Neutralizing capacity in mEq antacid is based on Fordtran's method; see footnote on page 113.

^c Cost is the list price in the 1974 *American Druggist Blue Book* plus standard 50% retail markup.

^d Titrilac also contains glycine.

^e Magaldrate is a chemical combination of aluminum and magnesium hydroxides.

acid regimen should be maintained for at least seven to ten pain-free days in the case of duodenal ulcers or until complete healing is demonstrated in the case of gastric ulcers.^{7,9} Intensive antacid therapy is especially important in gastric ulcer patients because acute gastric ulcers appear to heal significantly faster under antacid therapy.¹ Aggressive antacid therapy can also help lead the physician to an early decision on the possible malignancy of a given gastric ulcer.

A double dose of antacid at bedtime with or without an anticholinergic agent is often recommended, but there are no clinical data to support the increased efficacy of such a regimen. Antacid should be given to relieve typical ulcer pain as it arises between regularly scheduled doses.

There is considerable disagreement on antacid dosage to be used in clinical practice. Morrissey and Barreras advocate a low dose regimen in which 10 to 15 ml of an aluminum-magnesium hydroxide preparation is alternated every other hour with a constipating antacid.⁹ Fordtran recommends an hourly regimen in which 80 mEq (30 ml of Maalox[®]) is given for acute duodenal ulcers and 40 mEq is given

for acute gastric ulcers.⁷ Since the clinical efficacy of antacid therapy in the accelerated healing or prevention of complications of peptic ulcer disease has not been proved beyond doubt, the trade-off between adequate neutralization and bothersome side effects cannot be determined. Lacking such information, the physician should prescribe an antacid dose which falls between that advocated by Morrissey and Barreras on the one hand and by Fordtran on the other, but consistent with patient comfort.

RATIONALE FOR MASSIVE ANTACID THERAPY

Clinical²⁶ and experimental²⁷ evidence suggests that patients at high risk to develop gastrointestinal hemorrhage (e.g., patients in burn or trauma units) may be protected from stress ulceration and massive bleeding by constant gastric neutralization with high dose antacid. Randomized prospective studies are currently underway to resolve this issue. Recently, Curtis reported that uncontrolled bleeding stopped in 23 out of 25 patients with massive upper gastrointestinal hemorrhage when intragastric pH was held at 7 by the instillation of high dose antacid

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PROVIDER AND PROFESSIONAL RELATIONS MERGE

Maine Blue Cross and Blue Shield has merged its Provider and Utilization Review Department and Professional Relations Department to allow a more even flow of communications to all providers throughout the State. The new department will be called the Provider and Professional Relations and Utilization Review Department.

Rather than communicating with only one group of healthcare providers as they have been prior to the merger, the Administrators of Provider and Professional Relations will now be able to maintain close communications with all providers, including physicians, hospitals, dentists, pharmacists, and home care agencies. To allow for this cross communications, staff members that formerly conversed only with physicians will be visiting hospitals and those that were primarily concerned with hospitals will be meeting with physicians. This cross-training has already started and is expected to be completed by Fall 1975.

The merger will also allow for a more equal division of the State into geographic areas, resulting in better service to providers of healthcare.

PROMOTIONS ANNOUNCED

The Board of Directors of Maine Blue Cross and Blue Shield has announced the promotion of Thomas W. Cathcart from Director of Health Care Planning and Research to Vice President of Research and Provider Affairs. A graduate of Harvard, he joined Maine Blue Cross and Blue Shield as an Administrator of Professional Relations in 1969. Besides monitoring the activities of the newly-formed Provider and Professional Relations and Utilization Review Department, Cathcart will be responsible for the activities of the Health Care Planning and Research Department and the Maine Health Data Service. He is a member of the Maine Health Study Commission and the Joint Advisory Committee on ambulatory care in Cumberland County.

Laura P. Franciose, R.N., has been promoted to Director of Provider and Professional Relations and Utilization Review. She is a graduate of Mercy Hospital School of Nursing and St. Joseph's College, where she received her B.S. Prior to joining Maine Blue Cross and Blue Shield in 1972 as Coordinator of the Maine Blue Cross and Blue Shield Home Health Care Program, she was Coordinator of the Mercy Hospital Home Health Care Program. She is a member of the School Board for Holy Cross School and a member of the Board and the Executive Committee of the Maine Chapter of the Arthritis Foundation.

News, Notes and Announcements

Tufts University School of Medicine Office of Continuing Education

1975 Course Announcements

INHALATION AND RESPIRATORY THERAPY COURSE
(XIV): 7th Floor Lecture Hall, Tufts University School of Dental Medicine, April 21-25, 1975; 9-5

EARLY CARE OF THE SICK NEWBORN INFANT: Co-sponsored with St. Margaret's Hospital; Marriott Motor Hotel, Newton; May 9-10, 1975

A REVIEW OF RECENT ADVANCES IN INTERNAL MEDICINE: Marriott Motor Hotel, Newton; May 27-31, 1975; 8:30-5:30

GROSS AND MICROSCOPIC PATHOLOGY OF THE SKIN: In cooperation with the Department of Dermatology; Howard Johnson's 57 Park Plaza, Boston; June 9-13, 1975; 9-5

All courses and programs are accredited by the American Medical Association for the Physician's Recognition Award.

For additional information on individual courses and fees, please write to: Office of Continuing Education, Tufts University School of Medicine, Box 72, 136 Harrison Avenue, Boston, MA 02111. Telephone: (617) 423-4600, extension 309 or 310.

Seminar on Drug Therapy

"*The Focus on Pharmacy*" program of the Bingham Associates Fund will be conducting a seminar on drug therapy April 30, 1975. The program, intended for physicians, nurses and pharmacists, will feature presentations on anti-infective agents, analgesic therapy, psychotherapeutic agents, agents for arthritis and gout, total parenteral nutrition, and oncology therapy.

The meeting will be held at the Eastern Maine Medical Center in Bangor. Contact Mr. Robert Auger at Maine Medical Center in Portland, or Mr. John Kausch at Eastern Maine Medical Center, Bangor.

University Association for Emergency Medical Services

1975 Annual Meeting

May 20-24, 1975

Bayshore Inn, Vancouver, British Columbia, Canada

Fee: \$60; \$30 residents

Contact: Arthur E. Auer, Executive Secretary, P.O. Box 1241, East Lansing, Michigan 48823.

1976 Annual Meeting

May 10-16, 1976

University Hilton Hotel, Philadelphia, Pennsylvania

Contact: Arthur E. Auer, Executive Secretary, P.O. Box 1241, East Lansing, Michigan 48823.

Second Annual

Aspen Mushroom Conference

The Aspen Mushroom Conference is designed for physicians, scientists and amateur mycologists interested in the identification, toxic and hallucinogenic properties of mushrooms. The Conference is sponsored by the Beth Israel Hospital, Denver and the Colorado Mountain College, Glenwood Springs, Colorado and will be held at the Hotel Jerome, Aspen, Colorado, August 11-15, 1975.

An outstanding group of Colorado and visiting mycologists and physicians will serve as a faculty for the Conference. Didactic sessions and refresher courses on mushroom identification will be held in the early mornings and late afternoons at the novice and advanced student levels. Group discussions on advances in the diagnosis and treatment of mushroom poisoning will be offered to physicians and others interested in this subject. Gener-

ally, in the late summer, the Aspen mountains are richly productive of a wide variety of mushrooms. Experienced leaders will conduct daily forays into the surrounding mountains to collect edible and poisonous species and study their field characteristics.

For further information write to: Aspen Mushroom Conference, Registration Division, 3300 South Wabash Court, Denver, Colorado 80231, tel.: 303-755-2588.

5th International Congress of Electromyography

Dates: September 21, 22, 23, and 24, 1975

Place: Mayo Clinic, Rochester, Minnesota

Host Society: American Association of Electromyography and Electrodiagnosis (AAEE)

Organizing Committee:

Dr. E. H. Lambert (Rochester)

President of the Congress

Dr. W. R. Kennedy (Minneapolis)

Secretary of the Congress

Dr. J. Thomas (Rochester)

Treasurer of the Congress

Dr. R. J. Ellingson (Omaha)

Secretary, IFSECN

Dr. A. Struppler (Munich)

Chairman, EMG Commission IFSECN

Dr. W. C. Wiederholt (La Jolla)

Secretary-Treasurer AAEE (ex officio)

American Board of Family Practice

The American Board of Family Practice announces that it will give its next two-day written certification examination on November 1-2, 1975. It will be held at five centers geographically distributed throughout the United States. Information regarding the examination may be obtained by writing:

Nicholas J. Pisacano, M.D., Secretary
American Board of Family Practice, Inc.
University of Kentucky Medical Center
Annex #2, Room 229
Lexington, Kentucky 40506

PLEASE NOTE: It is necessary for each physician desiring to take the examination to file a completed application with the Board office. Deadline for receipt of applications in this office is June 15, 1975.

Mass Education Program to Combat Pinworms, Roundworms Launched by Roerig Division of Pfizer Pharmaceuticals

Combatting two major intestinal parasite problems of school-age children, pinworms and roundworms, is the subject of a sound-slide kit which can be borrowed, without charge, by groups of medical professionals and medical and nursing students. Physicians, nurses and health educators may also borrow the slides for showing to schools, parents' groups and other civic organizations.

Prepared by the Roerig Division of Pfizer Pharmaceuticals, the kit of more than 80 slides and a tape cassette is designed as a weapon in a campaign launched by Vivian K. Harlin, M.D., president of the American School Health Association. At the group's recent annual convention, Dr. Harlin, who is also director of health services, Seattle Public Schools, called for "a concerted attack on a problem that could affect as many as one-tenth of the nation's population*, the greater proportion of them children." She added that pinworms might be found to be even more prevalent if adequate screening programs were initiated to detect cases.

Dr. Harlin pointed out that some of the problems of pinworm or roundworm infection may be considered serious, while some

are merely troublesome and that "serious" could mean such clinical manifestations as pneumonia, perforated bowel, and bloody or mucous diarrhea. Also, some of the troublesome but less serious problems may be loss of appetite, insomnia, anal itch and irritability.

The president of A.S.H.A. also described the impact on a mother, "shocked to find that her child is infected or re-infected with those ugly crawling things. Then she becomes upset and angry because she has washed, chloroxed, boiled, brushed, vacuumed, air-dried, fumigated, and medicated the child, the clothes, the bedding, the brothers and sisters, and perhaps the cat and dog, only to find that the child is itching and scratching again and that flashlight examination of the anal region at night reveals that the pesky creatures are back again. It's a lot of work for a busy mother to treat for worms, to say nothing of the embarrassment she feels in having the school call this type of infection to her attention."

Beginning with the importance of hand-washing, and trimming the nails rather than biting them, the sound-slide presentation outlines personal hygiene, and housekeeping steps to break the cycle of reinfection. Curing an infected person begins with a

simple diagnostic test in which the anal area is swabbed with a scotch tape strip, which is examined under a microscope by a medical professional to detect pinworm eggs. A pleasant, single-dose treatment can then be prescribed by a physician.

To borrow a sound-slide set and obtain quantities of popularly written booklets on treating pinworms and roundworms, medical and nursing professionals and health educators may contact their local Roerig medical service representative or write on their letterhead to Roerig, Pfizer, Inc., 235 East 42nd Street, New York, N.Y. 10017.

*American Public Health Association Report, "Control of Communicable Diseases," statement to press by Warren Lawson, M.D., Minnesota State Health Commissioner, and statement to press by Richard I. Wenzel, M.D., Health Commissioner for Toledo and Lucas County, Ohio.

Involvement — Fulfillment

is our theme to apply. Have you as an Auxilian or the wife of a physician welcomed the new doctor and his family in your community with just a simple phone call?

JUNE M. FICKER
President

DRUG THERAPY REVIEWS — PHARMACOLOGY AND CLINICAL USE OF ANTACIDS

Continued from Page 114

per nasogastric tube.²⁸ Further confirmation of this clinical observation is awaited.

ACKNOWLEDGEMENT

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Necrologies

JOHN B. TITHERINGTON, M.D.

1919-1974

Dr. John B. Titherington, 55, a general surgeon who practiced in Portland, Maine from 1952 to 1965, died on November 25, 1974 after a long illness.

He was born in New York City on February 19, 1919, son of Richard H. and Kate G. Titherington.

A graduate of MIT, Dr. Titherington received his medical degree from Harvard Medical School in 1945. In addition to his medical degrees, he earned a degree in chemical engineering. After completing a surgical residency at Columbia Presbyterian Hospital in New York, he practiced in Portland and was a member of the medical staffs of the Maine Medical Center and the Mercy Hospital.

He resided in Falmouth and subsequent to his premature re-

tirement which was necessitated because of a series of disabling illnesses, he moved to Bremen and then to Union, where he resided at the time of his death.

Dr. Titherington was an affiliate member of the Cumberland County Medical Society and the Maine Medical Association. He was also a member of the American Medical Association.

Surviving are his widow, the former Trudy Grossman; a daughter, Miss Jeanne Titherington of Bremen; two sons, Geoffrey Titherington of Sanford and Gregory Titherington of Damariscotta; two stepdaughters, Miss Louise Grossman of Glen Cove, New York and Mrs. Amby Lyman of Patchogue, New York; a brother, William Titherington of Litchfield, Connecticut; and two grandchildren.

K. ALEXANDER LAUGHLIN, M.D.

1908-1974

Dr. K. Alexander Laughlin, 66, of Ontario, Canada, a Portland, Maine obstetrician and gynecologist for more than 30 years, died on December 12, 1974 in a Kingston, Ontario hospital after a week's illness.

Born in Gorham, New Hampshire on October 19, 1908, he was the son of Harry and Sadie Laughlin.

Dr. Laughlin was graduated from Portland High School and the University of Maine and received his medical degree from the University of Michigan Medical School in 1935. He interned at the Western Reserve Hospital and served a residency at Johns Hopkins. During World War II, he served as a Major in the U.S. Air Force as a flight surgeon in the Burma-China Theater. He

located in Portland in 1941 and moved to Ontario, Canada in January 1974 when he retired from active practice.

An affiliate member of the Cumberland County Medical Society and the Maine Medical Association, he was also a member of the American Medical Association, the Maine Obstetrics and Gynecology Society, and a diplomat of the American Board of Obstetrics and Gynecology. Dr. Laughlin was on the staffs of the Mercy Hospital and the Maine Medical Center.

Surviving are three sons, Kent A. of Newark, Delaware, Jeffrey S. of Portland, and Gary B. of Falmouth; two sisters, Mrs. Hazel Soule of Odessa, Ontario and Mrs. Olia Burt of Clearwater, Florida.

STELLA L. ULDALL, M.D.

1920-1975

Dr. Stella L. Uldall, 54, formerly of Augusta, Maine, died on January 6 in Houston, Texas.

Born in Zambales, Philippines on May 22, 1920, she was the daughter of Potenciano L. and Irene N. Lesaca.

Dr. Uldall was graduated from the University of Santo Tomas, Manila, Philippines and received her medical degree from the Faculty of Medicine and Surgery University of Santo Tomas in 1943. She interned at the University & Affiliated Hospital, served internships at the Woman's Hospital of Philadelphia and the Abington Memorial Hospital, Philadelphia, and took postgraduate courses at the Philadelphia General Hospital and the University of Indiana School of Medicine. Hospital appoint-

ments include the Institute of Juvenile Research in Chicago, the Clinica Santa Catalina, the University of the Americas, Mexico City, Mexico and the Devereux Schools in Victoria, Texas. In 1967, Dr. Uldall joined the staff as a psychiatrist at the Augusta Mental Health Institute, where she served until her resignation due to ill health in July 1974.

She was a member of the Kennebec County Medical Association, the Maine Medical Association, the American Psychiatric Association, and the Maine Psychiatric Association of which she was treasurer.

Surviving are a son, Robert Garcia; a daughter, Zenaida Blume; and a granddaughter, all of Houston, Texas.

STEPHEN S. BROWN, M.D.

1892-1975

Dr. Stephen S. Brown, 82, of Mars Hill, Maine, administrative director of the former Maine General Hospital from 1931 to 1949, died on January 19 at a Fort Fairfield hospital after a brief illness.

He was born in Calais, Maine on September 20, 1892, son of Samuel E. and Susan P. Brown.

Dr. Brown was graduated from the University of Maine and

received his medical degree from Tufts University School of Medicine in 1929. Following his internship and residency at the Maine General Hospital, Dr. Brown became acting director before assuming the administrative post. In 1949, he located in Mars Hill.

A senior member of the Aroostook County Medical Society

and the Maine Medical Association, he was also a former member and past president of the New England Hospital Association, a member of the American Medical Association, the American Public Health Association and the Maine Cancer Society.

WILLIAM L. CASEY, M.D.

1893-1975

Dr. William L. Casey, 81, of Cape Elizabeth, Maine, who had practiced in greater Portland for 50 years, died on January 24 after a long illness.

Born in Portland, Maine on September 6, 1893, he was the son of John D. and Ellen S. Casey.

He was graduated from Holy Cross College and received his medical degree from Tufts University School of Medicine in 1925.

Dr. Casey, a retired Colonel, commanded the 23rd Station Hospital, Seventh Army in World War II. After World War II, he

Surviving are a son, Stephen S. Brown, Jr. of Mars Hill; a daughter, Mrs. Robert Goss of Brandon, Vermont; a brother, Frank W. Brown of Ozona, Florida; a sister, Mrs. Janet B. Ryan of Mars Hill; and six grandchildren.

returned to Portland and resumed his practice and served as assistant city physician and Cumberland County medical examiner.

An honorary member of the Cumberland County Medical Society and the Maine Medical Association, Dr. Casey would have been eligible for his 50-year pin at the annual session this June.

His wife, the former Yvonne B. Fortin, died in 1965. Surviving are a son, William L. Casey, Jr. of Cape Elizabeth; a brother, John J. F. Casey of Portland; a sister, Miss Marion Casey of Cape Elizabeth; a granddaughter and several nieces and nephews.

JAMES A. WILLIAMS, M.D.

1881-1975

Dr. James A. Williams, 93, of Mechanic Falls, Maine and Westport Island, died on February 20 at a Lewiston hospital.

He was born in Topsham, Maine on October 26, 1881, son of Joseph M. and Elizabeth A. Williams.

Graduating from Brunswick High School, Bowdoin College in 1905 and Farmington Normal School in 1908, he served as principal of Lubec High School for two years and superintendent of schools in Millinocket and Patton for two years. In 1914, Dr. Williams received his medical degree from Bowdoin Medical School and then interned at St. Mary's Hospital in Lewiston.

Dr. Williams practiced in Readfield, South Gardiner and Jonesport, and in 1924 located in Mechanic Falls.

An honorary member of the Androscoggin County Medical Association and the Maine Medical Association, Dr. Williams received a 50-year pin in 1964, a 55-year pin in 1969 and a 60-year pin in 1974.

Surviving are his widow, the former Alice Blake; three sons, Richard A., Frank R. and Roger J., all of Mechanic Falls; a brother, Roger E. of Topsham; four grandchildren and a great-grandchild.

ACHSA M. BEAN, M.D.

1900-1975

Dr. Achsa M. Bean, 74, died on March 5 at her Lucia Beach residence on Ash Point, Owl's Head, Maine.

Born in Detroit, Maine on June 3, 1900, she was the daughter of J. Ralph and Florence E. Bean.

Dr. Bean was graduated from the University of Maine and received her medical degree from the University of Rochester School of Medicine in 1936. Following her internship and residency at Strong Memorial and Rochester Municipal Hospitals, Dr. Bean practiced at various hospitals in New York and was head of the medical department of Vassar College, retiring from that position in 1963. Since that time, she had made her home

with Dr. Barbara B. Stimson at Owl's Head.

During World War II, Dr. Bean served with the Royal Army Medical Corps, Great Britain, and received her commission as Major. In 1943, she transferred to the U. S. Naval Reserves, holding the rank of Lieutenant Commander.

A senior member of the Knox County Medical Society and the Maine Medical Association, she was also a member of the American Medical Association.

Surviving are a niece, Mrs. Charles Strohmeier of Reading, Pennsylvania; a nephew, Robert Bean of Augusta; and two grandnieces and one nephew.

RALPH P. EARLE, M.D.

1913-1975

Dr. Ralph P. Earle, 61, of Vinalhaven, Maine, who established one of the State's first regional medical programs in Vinalhaven, died on February 25 following a long illness.

Born in Philadelphia on August 15, 1913, he was the son of Ralph P. and Ida E. Earle.

Dr. Earle was graduated from Friends Central School in Philadelphia and the University of Pennsylvania, received his medical degree from Hahnemann Medical College in 1936, and interned at Hahnemann Hospital in Worcester, Massachusetts.

His first trip to Vinalhaven was on a family vacation in 1922. In

1932, he returned as a teenager to spend the entire summer and from then on came every chance he had. Vinalhaven was always on his mind and Dr. Earle set up practice in March of 1937. In 1942, he applied for a commission in the Army Air Corps and was assigned to the Air Transport Command. Back in Philadelphia by 1945, he was asked by the people of Vinalhaven to return. In 1946, the Islands Community Medical Service was established as a partially tax-supported, non-profit organization. By the 1950s, Dr. Earle established a regional medical program of preventative medicine, public health nursing service, a pharmacy, and a vari-

ety of clinics, as well as a diagnostic and treatment center. It was a decade later before the concept was adopted elsewhere in the State. Through Dr. Earle's efforts, assistance was obtained from the U. S. Government under the Hill-Burton Act to construct the present Islands Community Medical Center (ICMC), the only diagnostic and treatment center built under this program in Maine. Ever since its opening in 1962, it has operated in the black. "Pill Hill," as the islanders affectionately knew his clinic, stands as an example of what rural medicine should be, a monu-

ment to the dedication and skills of that one man.

Dr. Earle was a member of the Knox County Medical Society, the Maine Medical Association, and the American Medical Association.

Survivors include his mother, Mrs. Elizabeth Earle of Vin-alhaven; two brothers, Jack Earle of Baltimore, Maryland and Albert Earle of Mountainside, New Jersey; and several nieces and nephews.

County Society Notes

PENOBSCOT

The monthly meeting of the Penobscot County Medical Society was held on November 19, 1974 at Sing's Restaurant in Bangor, Maine, with 63 members in attendance.

The meeting was opened by the President, Dr. David M. Sensenig, and the minutes of the October meeting were approved as read.

Applications for membership into the County Society were received from Drs. Marshall Smith and Joseph Guaraldo. These were reviewed and approved by the Executive Council and subsequently these applications were unanimously approved by the membership.

A letter was received from Dr. Charles E. Burden of Bath, Maine concerning a new Blue Cross and Blue Shield 80% usual, reasonable, and customary policy. Dr. Burden objected to this policy on several grounds and requested that the County Society vote to reject this contract and resign from participation in the Blue Shield program if Blue Shield does not withdraw the contract. After discussion of this communication, it was requested that the representative from our district to the Executive Committee of the Maine Medical Association be instructed to inquire about this policy and report back to the membership at the next meeting. It was also requested that the secretary contact Blue Shield and request an explanation and more details of this new policy so that we may have more information available to us to judge the potential ramifications of this new policy.

There was no old business.

There was no new business.

Following the business meeting, the speaker for the evening, Dr. Irving Ariel, Clinical Professor of Surgery, New York Medical College, spoke on "Newer Knowledge Concerning the Natural History of Melanoma and Result of Treatment." Dr. Ariel provided a most interesting discussion concerning melanoma and the surgical treatment of this disease. A discussion period followed his presentation.

As there was no further business, the meeting was adjourned.

The monthly meeting of the Penobscot County Medical Society was held on December 17, 1974 at the Tarratine Club in Bangor, Maine. The meeting was opened by the President, Dr. David M. Sensenig.

The minutes of the meeting of November 1974 were read and approved.

A report to the membership of the recent meeting of the House of Delegates of the Maine Medical Association was given by Dr. Thornton W. Merriam, Jr. This report covered the various items of business discussed and transacted during the December 1974 meeting. The topic of Blue Shield's 80% Usual, Reasonable, and Customary contract was again discussed. This was discussed in detail at the House of Delegates meeting in December. A detailed discussion to the membership, however, was postponed until the January meeting when a representative of Blue Shield would be invited to attend and explain this policy and its ramifications more fully.

It was announced that the Nominating Committee of the Maine

Medical Association would meet on January 8, 1975, and if any member was interested in serving in a position or committee, to please notify the member of the Nominating Committee from this district.

By a vote of the membership, the request of Dr. Emilio Ocana to transfer membership from the Aroostook County Medical Society to the Penobscot County Medical Society was approved.

There was no new business.

Following the business meeting, the speaker of the evening, Mr. Eugene Cudworth, head of the medical malpractice division of the Hartford Insurance Company presented an up-to-date assessment of the status of malpractice across the country. He presented numerous examples of medical malpractice problems and how various states and parts of the country are dealing with this problem. After Mr. Cudworth's presentation, a lively question and answer session followed.

As there was no further business, the meeting was adjourned.

PHILIP G. HUNTER, M.D., *Secretary*

WASHINGTON

The regular meeting of the Washington County Medical Society was held on December 30, 1974 at the Peavey Memorial Library in Eastport, Maine, with seven members present.

The meeting was called to order by Dr. G. Bernard Shaw, President of the Medical Society.

Minutes of the last meeting were read and approved.

New Business:

1. Applications for admission to the Washington County Medical Society were reviewed. The following were admitted to membership: Drs. Ivan P. Markus of Machias and Rodney P. Ryan of Woodland.

2. Discussion of the new Blue Shield 80% Usual and Reasonable and Customary policy. Motion was made and passed that the sale and promotion of Blue Shield 80% Usual, Reasonable and Customary policy be dropped. The Blue Cross and Blue Shield will be so notified.

3. Next business was the discussion relative to the last meeting of the House of Delegates, held on December 14, 1974 at Bangor, Maine. Various items were discussed, including delegates' reports from the AMA. Drs. James C. Bates and A. Cowan Collins were set up as a committee to study the multiplicity of health systems in Washington County; also to further study the concept of a professional assistant to the Secretary of the County Medical Society.

A regular meeting of the Washington County Medical Society was held on January 27, 1975 at the Staff Lounge, Down East Community Hospital, Machias, Maine, with eleven members and guests present.

The meeting opened under the direction of Dr. G. Bernard Shaw, President of the Society.

1. Minutes of the last meeting read and approved.

11. Discussion by Dr. Robert G. MacBride, Delegate to the Maine Medical Association and Dr. Donald M. Robertson, alter-

nate delegate, in regard to the last meeting of the House of Delegates held in Bangor, Maine.

a. Discussed were reports of the AMA Clinical Convention; Dr. Robert F. McAfee, the official delegate mentioned the \$60.00 assessment the AMA plans to collect in an attempt to recuperate approximately \$3,000,000.00 deficit.

b. Also discussed was the Medical School for Maine. This was followed by general discussion on Malpractice Insurance with increasing rates that were affecting all members with apparent difficulty of various members in obtaining insurance, plus the strong possibility of the present rates being doubled within one or two months and again increasing difficulty in obtaining any type of Malpractice insurance.

Dr. James C. Bates reported on the concept of a professional assistant secretary to the Washington County Medical Society. He stated that as yet, they had come up with no concrete ideas. He stated that he and Dr. Arthur C. Collins would have more of a report on their progress at the next meeting.

The main business of the meeting was a discussion of the Constitution and Bylaws of the Washington County Medical Society that were first formulated in January 28, 1897 and the last change in 1908. It was moved and seconded and passed that the President appoint a committee to review the Constitution and Bylaws. Dr. Shaw stated that the committee would be furnished with copies of the present bylaws and efforts would be made to obtain copies of more up-to-date bylaws from other societies in the State. Members of the Society will meet with members from St. Stephen on February 4, 1975 and will attempt to revitalize the St. Croix Medical Society.

The next meeting will be at the home of Dr. A. Cowan Collins, Dennysville, Maine on February 24, 1975.

Meeting adjourned: 9:20 p.m.

KARL V. LARSON, M.D., *Secretary*

KENNEBEC

The Kennebec County Medical Association met at the Augusta Civic Center on December 19, 1974. The staff of the Augusta Mental Health Institute had a brief business meeting preceding the cocktail hour and dinner. Following this, the President, Dr. William E. Schumacher, presided at the business meeting. The minutes of the previous meeting were accepted as read.

The applications of two new physicians for membership in the Association were read. They were Drs. Marvin Eisengart and Dorothy Eisengart.

Dr. Schumacher then reported on the status of the revised bylaws. He discussed the section of the bylaws concerning due process which should include the following points:

A. A full and fair hearing should be insured the physician against whom a complaint is made. The President will be responsible for delivering a copy of the charge to the physician involved, urging that the problem be resolved by the physician with the complainant.

B. The President would then check to see if the charge was dropped or the problem resolved within 30 days.

C. If the charge is against a physician not a member of the county association, it will be referred to the Maine Medical Association or the Board of Medical Registration.

Dr. Francis J. O'Connor suggested that we get a legal opinion from the Maine Medical Association regarding this proposed change in bylaws. The members present approved this and Dr. Schumacher stated he would obtain this opinion.

Dr. Schumacher then suggested that the Association consider an Executive Secretary to handle the increased work that the activities of the Association seem to require. After some discussion, it was decided that a questionnaire be sent out to the membership to determine the posture of the Association, specifically whether the Association would be primarily a social and education organization or would become more involved in the socio-economic and political activities of medicine. Dr. O'Connor made a motion that the secretary write the congressional delegation regarding noise pollution. This was after an

announcement by Dr. Loring W. Pratt that the legislation that was proposed at the Federal level was in danger of passing without significant position control or input.

Dr. Richard I. Chamberlin gave a report of the House of Delegates' meeting held earlier in the month. There was some discussion of Mr. Nellson's report to the House of Delegates on the 80% UCR program. After some discussion, Dr. George I. Gould suggested that Mr. Nellson be invited to speak to the County Association and the secretary was instructed to extend an invitation.

Dr. Gould, as chairman of the Nominating Committee, presented a slate of officers as follows:

President: Dr. Joseph J. Hiebel, Waterville

Vice President: Dr. James C. Hayes, Augusta

Secretary-Treasurer: Dr. Oscar T. Feagin, Augusta

Council members: Drs. Richard E. Barron, Winthrop, Valentine J. Moore and John W. Towne, both of Waterville

Delegates to the M.M.A. House of Delegates: Drs. Earle M. Davis, Raymond E. Culver and Anthony Betts, all of Waterville, Terrance J. Sheehan, Augusta, George I. Gould, Richmond and Richard E. Barron. Alternates: Drs. Charles E. Towne, Antoine A. Atallah and J. Alfred Letourneau, all of Waterville, John H. Shaw and Harry M. K. Peddie, both of Augusta, and Howard H. Milliken, Hallowell

There were no further nominations from the floor, and the secretary was instructed to cast one ballot for the slate.

It was pointed out that an opening on the Executive Committee of the State Association would have to be filled in June and that the membership should be considering nominees for this position. Dr. Paul J. Jabar is a member of the Nominating Committee from Kennebec County.

Dr. Theodore J. Radomski then introduced the speakers of the evening, Mrs. Marilyn McInnis, Director of the State Office of Alcoholism and Drug Abuse Prevention, and Dr. Walter Christie, Assistant Professor of Psychiatry at Tufts University Medical School and Director of Resident Training and Research in Psychiatry at the Maine Medical Center. They presented an interesting program on people with alcohol problems. A lively question and answer period followed.

The meeting adjourned at 10:00 p.m.

KEVIN HILL, M.D., *Secretary*

The January 15th meeting of the Kennebec County Medical Association was held at the Silent Woman Restaurant in Waterville, Maine. Following cocktails and dinner, the President, Dr. Joseph J. Hiebel called the meeting to order.

Minutes of the previous meeting were dispensed with for the time being.

The application of Dr. Joseph R. Metz for membership in the Association was read. The Association unanimously accepted into membership Drs. Marvin Eisengart and Dorothy Eisengart.

The business portion of the meeting was devoted to a joint discussion with members of the Kennebec County Bar Association on the subject of the legal and medical definition of death. The discussion was ably led by Fouad Salim of the Attorney General's office and Dr. Irving I. Goodof. A most interesting discussion ensued. No particular conclusions were obtained.

O. THOMAS FEAGIN, M.D., *Secretary*

CUMBERLAND

The December 1974 meeting of the Cumberland County Medical Society was held December 19 at Valle's Restaurant. Eighty-five members were present. The dinner and service were of good quality.

Following the dinner, the business meeting was called to order by the President, Dr. Stanley B. Sylvester.

The minutes of the November meeting were read and accepted.

The application of Dr. John L. Newcomb was read for the second time and Dr. Newcomb voted into junior membership.

The Cumberland County representative on the 1975 Maine Medical Association Nominating Committee is Dr. Winton Briggs.

Resolutions on the deaths of Drs. Wilbur F. Leighton, Eugene E. O'Donnell and John B. Titherington were read.

A report on the recent meeting of the Maine Medical Association House of Delegates was presented by Dr. Douglas R. Hill.

Following this, Dr. Robert E. McAfee presented his report on the recent American Medical Association meeting in Portland, Oregon.

An announcement concerning the January 16, 1975 meeting at Union Mutual was made. Wives are invited as guests. The speaker will be Mr. Don Larrabee.

The business meeting was adjourned by Dr. Sylvester at 9:00 p.m.

Dr. Harry A. Bliss then presented his concepts of a free standing primary care health facility. Dr. Robert M. True then brought us up to date on the operations at the Model Family Practice Unit on Munjoy Hill.

ALFRED E. SWETT, M.D., *Secretary*

YORK

The annual meeting of the York County Medical Society was held at the Cascades Inn, Saco, Maine on January 8, 1975. It was a combined affair with the Woman's Auxiliary of the York County Medical Society.

The program was as follows: Social Hour — 6:30 p.m. to 7:30 p.m.; Dinner — 7:30 p.m. to 9:00 p.m.

The featured speaker of the evening was Ralph Ross of Sanford, Chief Judge of District Court, State of Maine. He gave an enlightening talk on District Courts of Maine. The talk was replete with humor and information.

The meeting was presided over by Dr. Carl E. Richards of Sanford, President of the York County Medical Society. Another feature following this was the introduction of many prominent guests and included Dr. and Mrs. John B. Madigan, President of the Maine Medical Association from Houlton and Dr. and Mrs. William O. Buell of Biddeford. Mrs. Buell is currently President of the Woman's Auxiliary of the York County Medical Society and was also in charge of the guest list.

Separate business meetings were presided over by the respective aforementioned Presidents.

The format of the Business Meeting of the York County Medical Society was as follows:

Call to order — Dr. Carl E. Richards, President.

Dispensing of minutes of last meeting and annual report.

Report of Nominating Committee — Dr. Melvin Bacon:

President: Dr. Carl E. Richards, Sanford

Vice-President: Dr. Thomas Anton, Biddeford

Secretary-Treasurer: Dr. Melvin Bacon, Sanford

Executive Committee (to include above officers): Drs. Robert S. Lafond, Saco and Walter R. Peterlein Jr., Springvale

Delegates to the M.M.A. House of Delegates: Drs. Carl E. Richards, Badi M. Haq, Biddeford and Maurice Ross, Saco. Alternates: Drs. Owen O. Dow, Kennebunk, Marcel P. Houle, Biddeford and Alexander W. Magocsi, York

Censor Committee: Drs. Marion K. Moulton, Chairman, W. Newfield, Roger J. P. Robert, Biddeford and Paul S. Hill, Jr., Saco

Peer Review Committee: Drs. Kenneth E. Leigh, Chairman, York, Harry Lapirow, Kennebunk and Conner M. Moore, Saco

Nominating Committee (for 1976): Drs. Melvin Bacon, Chairman, Charles S. Turville, Alfred and Ralph S. Belmont, Sanford

These nominees were elected to office for 1975.

Report of House of Delegates Meeting held in Bangor, Maine on December 14, 1974 was given by Dr. Carl Richards.

New Business: Dr. Thomas D. Chayka of York was voted into membership to the York County Medical Society. Also voted and passed was a resolution presented by Dr. Meredith Russell, Emergency Room Physician, Webber Hospital, Biddeford. It read as follows: "Sec. 74. Transportation to Hospital. Amend by adding at the end of the section, 'Ambulance personnel may continue to render emergency treatment at the hospital under the direction and control of a licensed physician until such time as in the opinion of such licensed physician there is no further need for such treatment by said ambulance personnel.' " This is part of the ambulance service chapter of Title 32.

Announcement of Program for 1975:

March 12, 1975 — Goodall Hospital, Sanford

May 14, 1975 — Webber Hospital, Biddeford

October 8, 1975 — York Hospital, York

January 14, 1976 — Annual Meeting (location to be announced later)

Meeting adjourned.

Dancing followed with music by Syd Lerman and his orchestra of Portland, Maine.

This truly was a gala affair with 94 doctors and wives and guests present. It is also worthy of mention that Dr. Carl Richards was reelected to the Presidency of the York County Medical Society and his 33rd term as a Delegate to the Maine Medical Association.

This affair ended at midnight and was enjoyed by all.

MELVIN BACON, M.D., *Secretary*

LINCOLN-SAGADAHOC

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at the Ledges in Wiscasset, Maine on January 21, 1975.

The meeting was called to order at 8:40 p.m. by the Vice-President, Dr. Ralph C. Powell. The minutes of the December meeting were read and accepted as read.

Dr. Powell then turned the meeting over to Dr. Louis Bachrach of the scientific program committee, who introduced Dr. Galen Johnson of Brunswick. Dr. Johnson spoke on Carotid Artery Disease.

Old Business: None.

New Business: None except reports of proposed legislative actions.

Committee Report: Treasurer's Report accepted as printed. The Nominating Committee Report was read by Dr. John F. Dougherty:

President: Dr. Ralph C. Powell, Damariscotta

Vice-President: Dr. David S. Hill, Bath

Secretary-Treasurer: Dr. George W. Bostwick, Newcastle
Delegates to the M.M.A. House of Delegates: Drs. Anthony J. Horstman, Boothbay Harbor and David W. Schall, Brunswick. Alternates: Drs. Frank O. Avantaggio, Jr., Damariscotta and Gilbert R. Rowan, Bath.

Censors: Drs. Samuel L. Belknap, Damariscotta, John F. Dougherty, Bath and Carl R. Griffin, Jr., Boothbay Harbor

Diabetes: Dr. Robert M. Hassan, Damariscotta

Scientific Program: Drs. Robert H. Dixon and Paul H. Dumdey, both of Bath.

The motion was made that the nominations be closed and that the secretary cast one vote for the entire slate as presented. The motion was seconded and passed unanimously.

Dr. Paul A. Fichtner mentioned some bills now before the State legislature, especially regarding generic prescribing. Dr. Peter A. Evans reported the PSRO decisions of Regional Memorial Hospital. Dr. David W. Schall mentioned the possibility that the State Department of Health and Welfare will discontinue providing free laboratory services. Comment was generated. The suggestion was made that legislature committee reports be sent to each hospital staff in the area.

GEORGE W. BOSTWICK, M.D., *Secretary*

Letter to the Editor

To the Editor:

Two new medications, Aarane (Syntex), and Intal (Eli Lilly) have been on the market for over a year, both are Chromolyn Sodium, which are administered by an inhaler. They are usually prescribed q.i.d. for people who suffer from bronchial asthma on a perennial, or seasonal basis. These have been very effective if used with proper instruction by the physician to the patient and in the proper dose for symptomatic relief and prevention of asthmatic attacks. However, they do not have any effect on the body's immune system. They are certainly no substitute for proper medical work-up of a patient who has symptoms of wheezing, and certainly, in many cases is not a substitute for allergy desensitization, or hyposensitization, now called Immuno-Therapy. Depending on where you obtain Aarane or Intal, the cost varies, but the average cost is 25¢ per capsule, or \$1.00 per day for treatment.

In writing this letter, I am suggesting that anybody who prescribes this medication, to consider the cost, as well as the indications, and realize that it is only for relief of the symptoms of wheezing, and prevention as long as it is used, and effective if used properly in an unpredicated number. Most important, it is not a cure.

I have seen many patients directly, and have heard about several indirectly, who have been placed on this medication because of wheezing, which is due to irreversible lung disease, and other non-allergic asthma cases, and continued to be used despite no relief after 4-6 weeks. In such instances, these medications are unlikely to result in good results, or relief of symptoms, however, this does not contra-indicate a therapeutic trial of 4 weeks, in many instances. However, if no effect is seen after that period of time, it is very, very unlikely that relief will be seen.

The use of Chromolyn Sodium is alleged to inhibit the degranulation of sensitized mast cells which occurs after exposure to

specific antigens and inhibits the release of histamine, and slow re-acting substances -A from the cells lining the bronchial tree, and therefore, most effective in situations where these are the chemical mediators of asthma, and hence more effective in allergic asthma, or reversible lung disease rather than in chronic obstructive lung disease and other causes of wheezing, in which it may be ineffective. Chromolyn Sodium has no *intrinsic* bronchodilator, antihistamine, or anti-inflammatory activity.

Patients who have allergic asthma should be placed on Aarane, and/or Intal to tide them over a seasonal problem, or perennial problem until Immuno-Therapy can be instituted, and evaluated in helping the patient. Certainly this type of therapy should not be prescribed for every patient who has mild asthma, i.e., a few attacks per year, which may often be associated with bronchitis and can usually be controlled with bronchodilators, and antibiotic and an expectorant.

Most allergists are selective in their choice of patients for whom they prescribe Chromolyn Sodium and have been very successful in reducing steroid dosage in patients who could not be maintained on the usual medications, and allergy desensitization, as well as environmental control. Chromolyn Sodium has helped many patients, who suffer from allergic bronchial asthma, but since it is relieving the symptoms of wheezing as long as taken, and is not treating the disease, it is no substitute for allergy work-up, and if indicated, Immuno-Therapy.

As physicians, we must dedicate ourselves to the relief of the symptoms, but more importantly, the treatment of the basic disease process which in allergic disease is based on the understanding and knowledge of Immunology.

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Letter to the Editor

To the Editor:

MAY IS NATIONAL HIGH BLOOD PRESSURE MONTH

A Report on Community Hypertension Screening in Maine

Recent studies document that hypertension is a risk factor in the development of strokes, heart diseases, and heart and kidney failures. They also indicate that controlling hypertension is an important factor in preventing these failures. This has inspired a number of Maine organizations to screen the general population for high blood pressure.

A Medical Care Development, Inc. survey, conducted under contract for the Maine Department of Health and Welfare, revealed that fifteen community screening projects screened 18,000 Maine residents in 1974. The projects had developed independently of one another and possessed different procedures and referral criteria. Ranges of referrals varied from 8% in Belfast where the cutoff was 170/90 to a 42% referral rate in Kennebunk where a 160/90 cutoff point was used. The referral rates were also dependent on such factors as how many were already under adequate treatment and the age of those being screened. In a 2,700 person Statewide sample, the Maine Heart Association, which uses a 160/95 cutoff point, found 21% of the sample population needed referral for further diagnosis. This figure lies above the national average (10-15%) for the white population.

Seven senior citizens programs check blood pressures either separately or as a component of multiphasic screening activities. About 4,500 senior citizens, primarily from south central Maine, are checked yearly via such facilities. Other programs open to the general public operate through a number of organizations including the Seventh Day Adventists, Lions Club, Public Health Nursing, hospitals, United Way, Maine Heart Association, and Franklin County High Blood Pressure Program.

Costs differ among these organizations depending on whether volunteer or reimbursed help is utilized. Nurses perform most of the screening and follow-up activity, although other types of health personnel are used. Follow-up procedures vary considerably. The most standard technique is to tell potential hypertensives that they should visit their physicians and, at the same time, send the doctor a letter informing him of the reading. More complex methods provide for phone calls, letters, and visits to physicians and clients to ensure follow-up.

Clearly, there is a lack of uniformity among programs which severely complicates specific definition of the problem in Maine.

As a response to publicity about High Blood Pressure Month, a number of groups have indicated a desire to develop screening programs. An ad hoc meeting consisting of representatives of the Department of Health and Welfare, Maine Heart Association, and Medical Care Development, Inc. is attempting to support and coordinate activities for the month. Interested parties can now request a "Guide to Community Blood Pressure Detection and Control," which suggests systematic criteria for referring clients and a single point determination of over 160/95 for groups unable to handle a more complex program. In addition, all screening program organizers are asked to collect specific data, fill out an amalgamized survey, and send it to a central address where the information will be compiled to further define the problems in Maine.

This plan has been endorsed by a number of health organizations, and by adhering to the guidelines, local screening projects automatically can cite the endorsement.

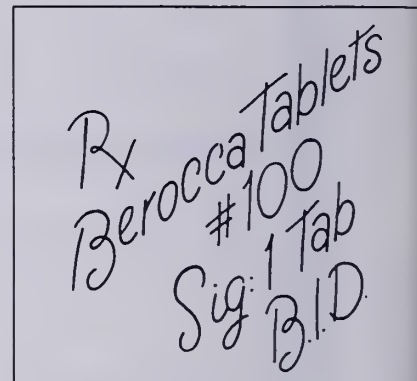
Guidelines and surveys are available through Ellen Baum, Screening Consultant, c/o Medical Care Development, Inc., 295 Water Street, Augusta, Maine 04330.

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The Journal of the Maine Medical Association

Volume Sixty-six

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Number 5

Health Care Delivery in Maine I: Patterns of Use of Common Surgical Procedures

JOHN E. WENNBURG, M.D.* and ALAN GITTELSON, Ph.D.**

We report herein patterns of use of surgical procedures among geographically distinct Hospital Service Areas in the State of Maine. Our purpose is to measure differences in the use of surgical procedures throughout the State and to discuss possible causes and implications. The data are presented as age-adjusted incidence rates by area for all surgical discharges and for the nine common surgical procedures: tonsillectomy, hysterectomy, dilation and curettage of the uterus, appendectomy, cholecystectomy, inguinal hernia repair, prostatectomy, hemorrhoidectomy and stripping of varicose veins. Surgical incidence rates in Maine and Vermont are compared. The cost implications of differences in use of surgery are considered. Patterns of intra-area differences in use of surgery are studied.

METHODS

Measurement of the per capita use of surgery is based on the cooperation of all hospitals in Maine in providing a uniform discharge abstract for each patient. The hospital record contains information on diagnosis, operative procedures and the patient's age, sex, and town of residence.† All abstracts of discharges occurring in the calendar year 1973 have been assembled in a single data file. Two distinct steps have been undertaken, the first to group towns of residence into Hospital Service Areas and the second to compute the incidence rates by area.

Definition of Hospital Service Areas. Like most New England states, Maine is well situated for small area analysis of health care delivery. The

State is organized administratively into over 500 towns which average about 36 miles in area. Geographic areas for study were defined by assigning each of Maine's 500 towns to a unique Hospital Service Area (HSA). A simple procedure was followed: Patient records were classified initially by town and hospital and towns were then assigned to the hospital used by the plurality of residents. To avoid possible confusion between mailing address and town of residence, zip code-town border relationships were investigated to make certain that no town was assigned to an HSA that did not contain its post office. Forty-two areas were defined; 35 areas contain a single hospital, 4 contain two; two contain three, and one contains four hospitals. The population size of the 42 areas ranges from 1,080 to 170,879. Five areas have more than 50,000 persons; 13 more than 20,000; there are 12 areas with populations between 10,000 and 20,000; 17 areas have less than 10,000 inhabitants.

Calculation of utilization indicators. In this analysis, rates of individual procedures are presented for the areas with 20,000 persons or more. These areas are shown in Figure 1. The extreme rates in surgical discharges are presented for smaller areas. For a study of patterns of intra-area variations, the five largest HSAs are used. The 1970 census populations for each town (grouped into HSAs) serve as the basis for computing surgical procedure rates. The numerators include resident surgical cases irrespective of whether the procedure was performed in or out of the area, and the rates therefore estimate the total incidence of surgery. Age adjustment to Maine population permits direct comparisons of areas with differing age structure (thus eliminating age as a possible explanation of differences). Admission to hospitals for materni-

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**Professor of Biostatistics, Johns Hopkins School of Hygiene and Public Health.

†Records contain no information identifying individual patients.

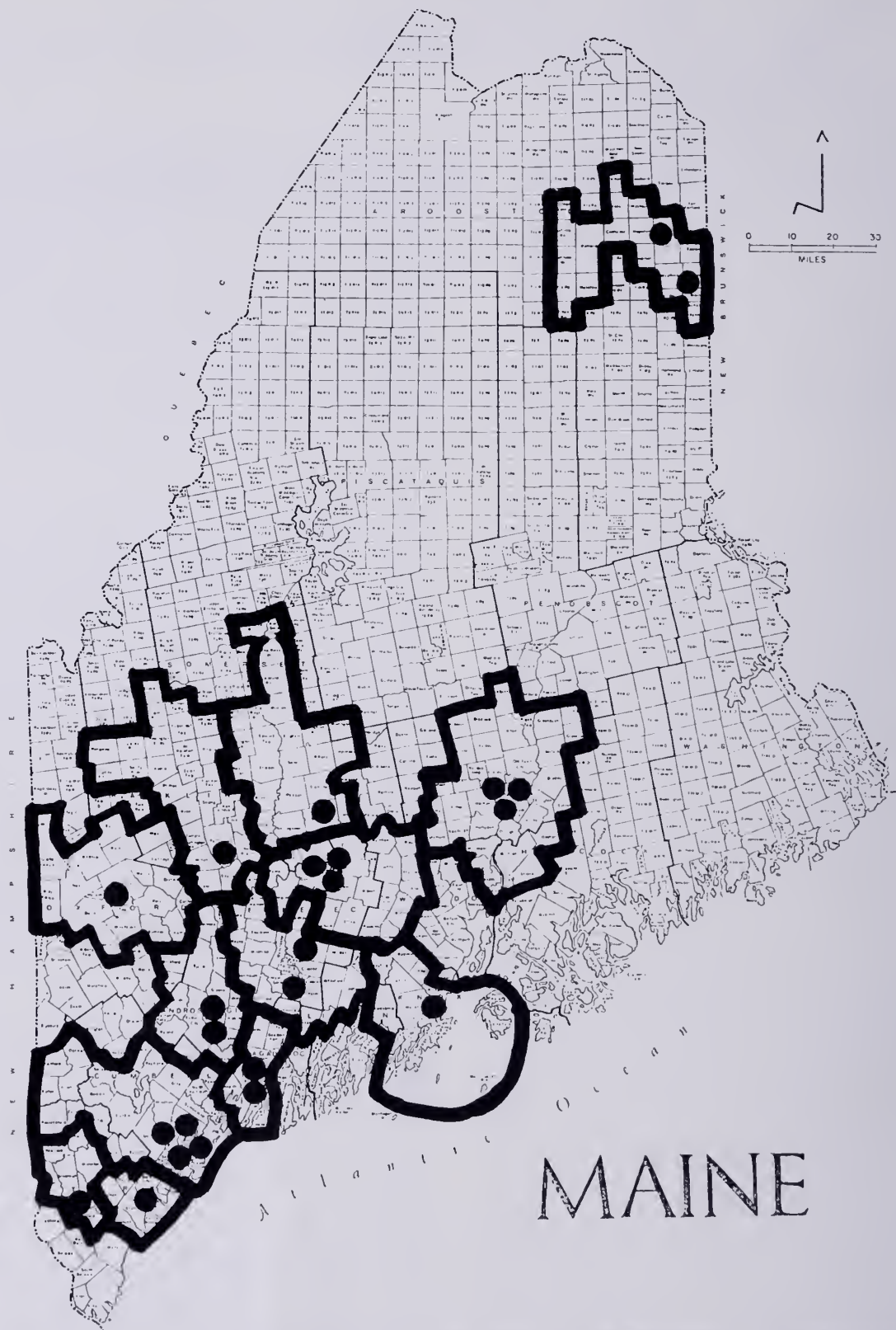


Fig. 1. Map of Maine showing minor civil divisions, the Maine town (lighter line). Darker line shows boundaries of Hospital Service Areas which contain the principal populations studied in this article. Circles represent hospitals.

TABLE 1
PERCENTAGE OF ALL RESIDENT SURGICAL PROCEDURES
PERFORMED AT LOCAL HOSPITALS: FIVE LARGEST
MAINE HOSPITAL SERVICE AREAS, 1973

Procedures	ICDA Code	Area I	Area II	Area III	Area IV	Area V
All		96	87	75	93	92
Tonsillectomy	21.1-21.2	98	86	78	98	95
Appendectomy	41.1	94	91	82	94	91
Hemorrhoidectomy	51.3	95	95	87	98	89
Hernia	38.2	96	87	87	93	92
Prostatectomy	58.1-58.3	98	94	29	94	98
Cholecystectomy	43.5	97	92	88	94	96
Hysterectomy	69.1-69.5	97	95	67	95	94
D & C	70.3	97	90	81	92	94
Varicose Veins	24.4	98	85	93	97	95

TABLE 2
1973 AGE-ADJUSTED INCIDENCE OF SURGICAL DISCHARGES AND NINE COMMON PROCEDURES IN MAINE AND
MAINE HOSPITAL SERVICE AREAS WITH POPULATIONS OF 20,000 OR GREATER. PROCEDURES PER 10,000 POPULATION.

Area	All Surgi- cal Dis- charges	Append- ectomy	Pros- tatec- tomy (males)	Inguinal Hernia (males)	Hyster- ectomy (females)	Vari- cose Veins	Hemorr- hoidec- tomy	Dilation & Curettage (females)	Tonsil- lectomy	Cholecys- tectomy (females)
State as a whole	689	17	25	45	59	5	7	77	62	35
1	613**	18	18*	40	46**	4	6	58**	36**	37
2	670	11**	22	37	59	6	3*	86	23**	46*
3	742**	13**	35**	47	63	4*	4**	83*	54**	33
4	606**	17	28	45	41**	3	5	49**	47*	36
5	594**	14	18	45	48	6	5	84	35**	31
6	640*	21	26	51	47	6	6	87	60	35
7	688	17	27	49	93**	6	9*	76	59	34
8	738**	17	40**	45	67	4	7	117**	55	50**
9	688	15	20*	53	39**	10**	9	74	62	29
10	864**	19	25	52	58	5	9	114**	105**	55**
11	954**	22**	33**	49	60	8*	19**	86	122**	39
12	579**	19	18**	35**	51**	5	5**	67*	77**	28*
13	764**	19	31	60*	48	7	14**	78	77**	27

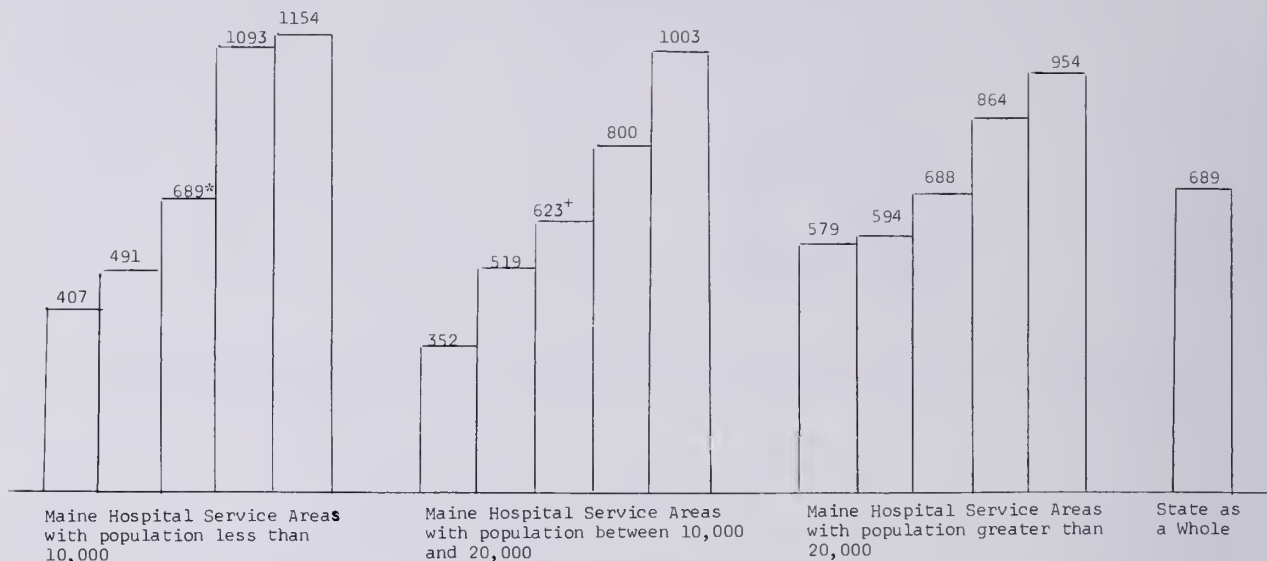
*Chi-square significant at the .05 level

**Chi-square significant at the .01 level

ties and common surgical and medical treatments tend to be highly localized. For example, in the five largest HSAs between 75 and 96 percent of resident discharges for surgery were from local hospitals (Table 1). For the individual procedures studied in this report, outmigration of resident population for more than one-third of services occurred in only one area (area III) and for only one procedure (prostatectomy). For most procedures in most areas, over 90 percent were performed in local hospitals. There is thus a close correspondence between the medical community of an area and the residents hospitalized from that area. Because of small size of the HSAs (and the absence of significant regionalization), a relatively small cohort of physicians are the dominant suppliers of medical services to the resident populations and their decisions can be studied by observing population-based rate profiles.

Statistical analysis and comparisons. The International Classification of Disease Codes for the pro-

cedures under study are presented in Table 1. Statistical differences among HSAs are based on Chi square distributions with one degree of freedom with the null hypothesis stating that an individual area does not differ from the State average rate. Comparisons between Vermont and Maine are based on the 13 largest hospital service areas in each state. The number of person-years of experience in the smallest Vermont area is 28,700; among Maine areas, the minimum number is 20,980. Vermont data are from a published source¹ providing rates for 1969-1971. The Vermont rates have been age-adjusted to the Maine population by the direct method of age-adjustment. In the study of intra-area patterns of variations, for each of the nine procedures, the ratio of the observed to the expected number of cases is used as a standardized index of incidence with the State average serving as the standard. The expected number of cases within each HSA was obtained by multiplying the population in each age group by the corresponding State-



* area ranked 9th out of 17

+ area ranked 7th out of 12

Fig. 2. Variations in Age-adjusted Surgical Rates Among Two Highest, Median, and Two Lowest Ranked Areas. 1973. Maine Hospital Service Areas Grouped by Population Size. Surgical Discharges per 10,000 population.

wide age specific rate and summing the age-specific expected number of cases across all age groups. Estimates of expenditures are based on State-wide average cost per case by hospitals participating in Maine Data Service; physician costs are computed using California Relative Value Index (one 1969 California Relative Value Unit = \$25.00).

RESULTS

Variation in age-adjusted incidence of surgery in Maine. Figure 2 shows the range of age-adjusted rates for all operative procedures. Among HSAs with more than 20,000 residents, the lowest rate of surgical discharges is 579 per 10,000 per year and the highest is 954 per year, 65 percent over the lowest. The intermediate size group of HSAs shows a low area rate of 352 per 10,000 per year and a high of 1003 per year — very nearly a three-fold difference. Among areas with smaller populations, the lowest observed rate of surgery is 407 and the highest is 1154 procedures per 10,000. Table 2 lists incidence rates for each of the nine common surgical procedures in each of 13 largest HSAs. For each procedure, there are areas with incidence rates that are statistically different than the State average. Repair of inguinal hernia shows the least number of statistical outliers (2); tonsillectomies show the most (9).

Comparisons among Vermont and Maine Hospital Service Areas. Figure 3 provides a comparison

of the Vermont and Maine surgical experience for the nine procedures. The 13 areas in each State with more than 20,000 population are used in this comparison. The pattern is one of wide variations both within and between the two States with tonsillectomies and vein stripping showing the greatest difference in state averages. Relative to population size, 37 percent more tonsillectomies are performed in Maine than in Vermont while 80 percent more varicose vein procedures are done in Vermont than in Maine. Intra-state variations in tonsillectomy rate are greater in Vermont, the lowest and highest areas being in this state. While hemorrhoidectomies are performed at approximately the same rate in both states, intra-state variations are much greater within Maine and the highest Maine rate exceeds the highest Vermont rate by 90 percent. Hysterectomies are performed 40 percent more commonly in Maine than Vermont, and the range across the high Maine area and the low Vermont area is over three-fold. Appendectomies and prostatectomies occur slightly more often in Vermont than in Maine but individual areas vary considerably: the ratio of difference for appendectomies between highest and lowest areas is 2.9; for prostatectomies it is 2.6. Although cholecystectomies and dilation and curettage are more common in Maine, intra-state variations are greater in Vermont. Hernia procedures show the least variation. The State averages are nearly identical and the intra-state differ-

TABLE 3

EXPENDITURES FOR NINE COMMON PROCEDURES IN AREAS WITH HIGHEST AND LOWEST INCIDENCE RATES, THIRTEEN LARGEST MAINE HOSPITAL SERVICE AREAS, 1973. COMPARED TO STATE AVERAGE.

Procedure	High Use Area ¹	Low Use Area ¹	State Average
Hysterectomy	\$ 6.78	\$ 2.88	\$ 4.30
Cholecystectomy ²	4.98	2.51	3.46
Prostatectomy	3.54	1.47	2.34
Tonsillectomy	4.55	0.85	2.33
Hernia ³	2.51	1.64	1.99
Dilation and Curettage	2.68	1.08	1.82
Appendectomy	1.99	0.97	1.47
Hemorrhoidectomy	1.43	0.23	0.54
Varicose Veins	0.93	0.30	0.48
All Nine Procedures	29.39	11.93	18.73

¹areas ranked independently on each procedure

²for females only

³for males only

ence among HSAs is the least for this procedure.

Dollar implications of variations in incidence of surgery. Variability in use of specific procedures reflects in expenditures. For the 13 largest Maine HSAs, Table 3 estimates the per capita expenditure for each procedure in areas of high and low use. The nine procedures in the areas of highest incidence cost a total of \$29.39 per capita. The corresponding figure for the low incidence rates is \$11.93, nearly a 2.5 fold difference. Of the individual procedures, tonsillectomy shows the greatest range of difference in per capita expenditure. In the low use area, \$.85 is expended per capita annually; in the high case area, \$4.55 is expended.

The data can be used to estimate the total costs in Maine for use of the procedures and to study the cost implications of generalizing across the State as a whole the high or, alternatively, the low strategy for allocating the nine procedures.* For the nine procedures, an estimated 18.0 million dollars were expended in Maine in 1973. If the high use strategy were the "medically" necessary level of care, at 1973 average costs it would take an additional 10.2 million dollars to meet this need. On the other hand, if the low use strategy were generalized, 6.6 million less than was expended in 1973 would be needed for these nine procedures. Again, the cost implication of tonsillectomy stands out: currently about 2.1 million dollars are expended annually for tonsillectomies. If tonsillectomies were performed everywhere in Maine as frequently as in the high use area, an additional 2.2 million dollars would be expended. If tonsillectomy use as observed in the low area were generalized, the estimated reduction in surgical costs in Maine is 1.4 million dollars annually.

*Statewide estimates are made by multiplying area per capita expenditures by 1970 populations of Maine.

Intra-area patterns of variation in incidence. Figure 4 shows the relative rate of use of total surgery and of selected common surgical procedures within the five largest Hospital Service Areas in Maine. Patterns of use of specific procedures within and among areas can be easily compared because area procedure rates are expressed as the ratio of area to Statewide average incidence rate. The figure shows that the rates at which specific procedures are performed within an area vary markedly and to a large degree independently of the total operation rate. For example, while area II and area III have the same total operation rate, area II exceeds in hysterectomies (doing 56 percent more than the State average) and area III exceeds in varicose veins (doing 84 percent more than the State average). In contrast, in area III, the hysterectomy rate is well below the State average and one-third the rate in area II. Of the five procedures, in each of the five areas a different procedure is performed most often; in four of the five areas, the least performed procedure is different.

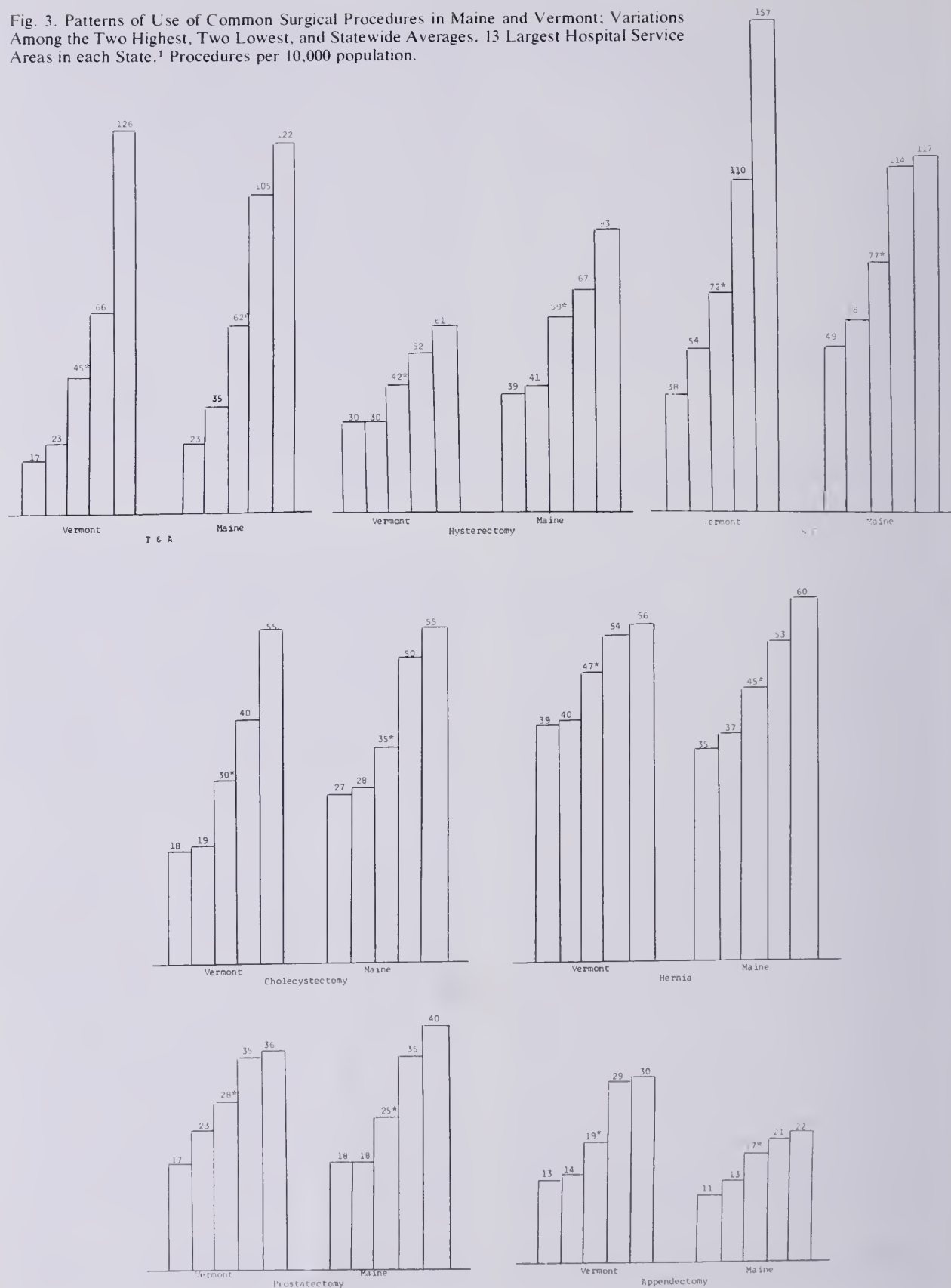
DISCUSSION

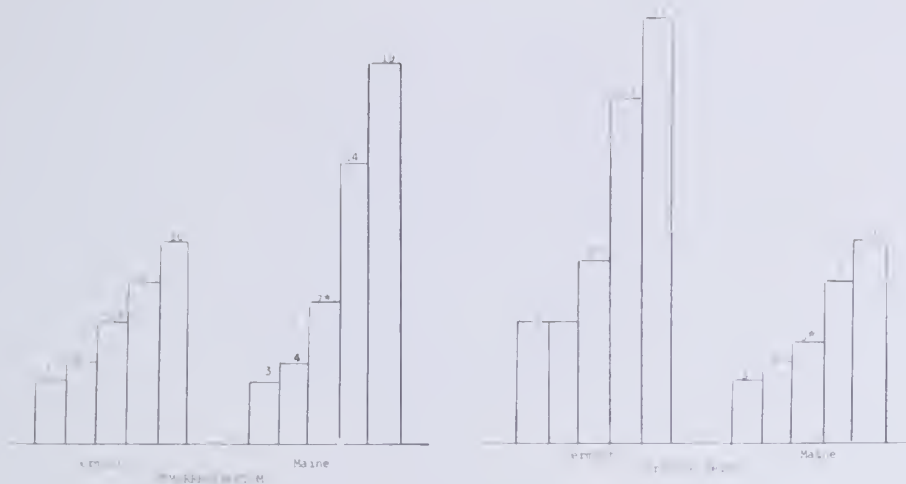
Variation among geographic areas are the rule. The findings of this study are consistent with previous studies of the incidence of surgery among geographically defined populations. Variability in use of procedures has been documented across national boundaries; Bunker² has shown the incidence of common surgical procedures in the United States to be double that of the United Kingdom. Lichtner and Pflanz³ found appendectomy rates in West Germany nearly three times the United States rate. Vayda and Anderson have recently demonstrated that the extreme rates of incidence of common procedures vary about two-fold across Canadian Provinces.⁴

It has become clear that variations among neighboring communities are also extensive. Lembcke's⁵ finding of differences in common procedures among Rochester suburbs (neighboring communities with apparently homogenous populations) have been substantiated in Kansas⁶, in Vermont⁷, and, with this study, in Maine. Small area geographic variations in use of surgical procedures are a rule for which there is yet no exception.

Variations in incidence of surgery reflect the distribution of physicians and facilities. The incidence of illness, socio-economic circumstances, the number and kinds of physicians doing surgery, the organization of care and methods of payment for service have each been postulated as reasons for geographic variations. While each factor undoubtedly contributes in some degree to patterns of health care consumption, the thrust of the evidence is that supply factors are more important than consumer behavior in determining the relative rates of use of

Fig. 3. Patterns of Use of Common Surgical Procedures in Maine and Vermont; Variations Among the Two Highest, Two Lowest, and Statewide Averages. 13 Largest Hospital Service Areas in each State.¹ Procedures per 10,000 population.





¹Vermont data are for years 1969-71 — Maine data are for 1973
 *State average

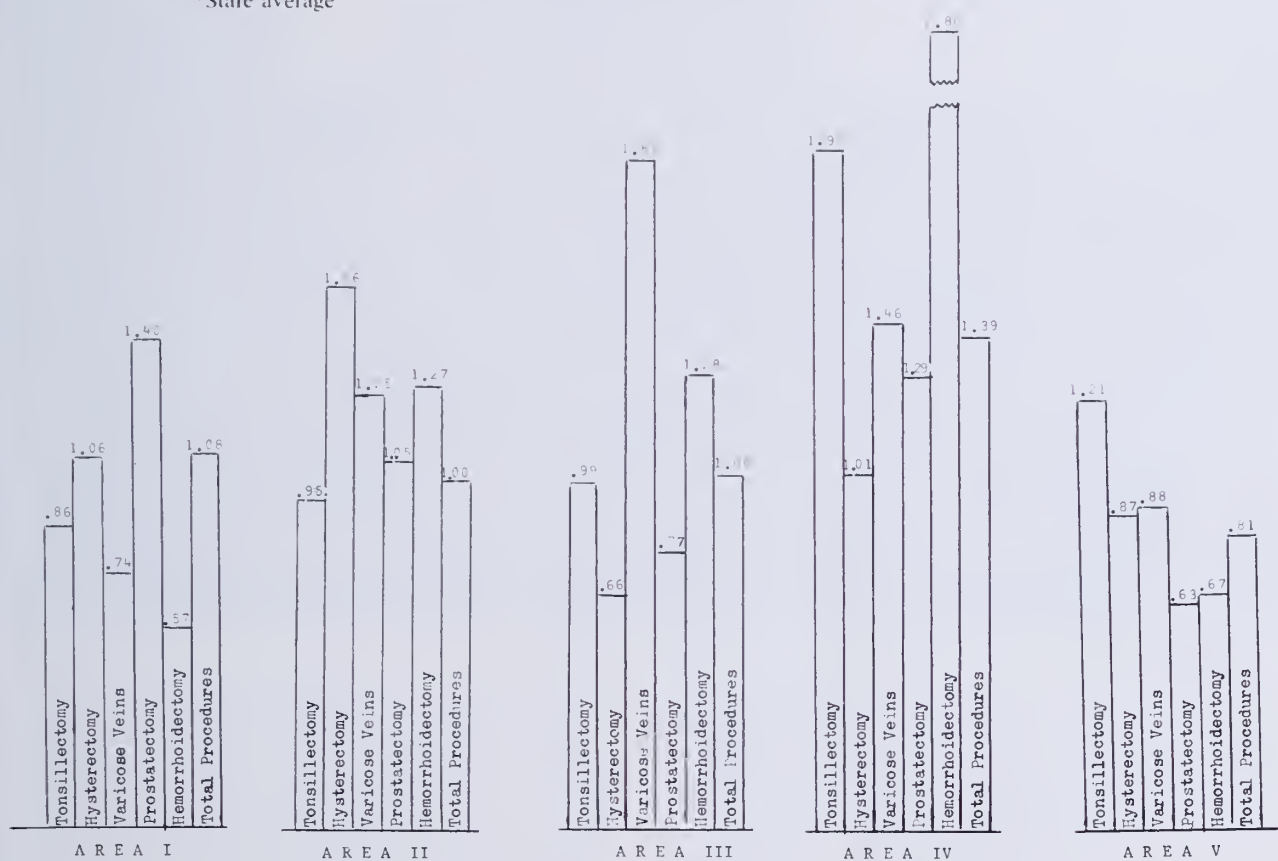


Fig. 4. Patterns of Intra-area use of Surgical Procedures: Ratio of Observed to Expected Number of Cases in 1973 for All Procedures and for 5 Common Surgical Procedures; 5 Maine Hospital Service Areas with population greater than 50,000.

surgical care among neighboring geographic areas. Studies in Kansas,⁶ Vermont,⁷ and across Canadian Provinces⁴ show that overall supply of surgeons and hospital beds are important statistical correlates with the incidence rates of surgery. In each of these studies, insurance coverage, method of payment (fee-for-service) and the basic method

of organization of practice were similar among the areas studied. Age-adjustment of incidence rates minimized the contribution of age-related illness rates as a possible explanation of differences in use care; in Vermont, additional studies of the population-at-risk have been undertaken; a household survey shows that the population of the HSA with the

highest and with the lowest rate of surgery have similar rates of illness, income, racial and social background, and insurance coverage; in fact, residents from these two HSAs contacted their physicians in equal portions on an annual basis and for episodes of acute illness.⁸

Formal surveys have not been undertaken among Maine HSAs to determine if the constituent populations vary in their need, ability or wish to consume health care. However, the pattern of variations suggests that as in Vermont and Kansas, population differences are not the important reason for variations. Patterns of variations in the five largest HSAs in Maine illustrate this point best. These areas are contiguous and sufficiently large so that chance variations are not plausible explanations for patterns of surgery incidence. In three of the areas, the overall rate of surgery is similar. Yet from area to area, the pattern of allocation of surgical technology is not consistent. The procedure performed most commonly is different in each area; the procedure least often used is different in four of the five areas. Remuneration to the surgeon for surgical work is standardized across areas and is based, primarily, on time surgeons spend in the operating room.⁹ It is, therefore, not at all clear that there is an economic incentive for physicians to select one procedure over another. A similar intra-area pattern of allocation was observed among Vermont areas. We suggest this variety in use of specific technology reflects differences among physicians in their belief about effectiveness or in their judgments concerning how health care needs are defined.

Strategies for reducing uncertainty. The bases for differences in professional opinions on use of procedures are complex. In some instances, they undoubtedly involve differential diffusion of knowledge on the indications for treatment or the value of the procedure. Particularly in these cases, feedback of information to physicians on the population incidence rate may serve as an impetus for review of the indications for procedures. There are indeed a few examples where such feedback may have had some effect on rate of use. Lembcke⁵ demonstrated changes in incidence of pelvic surgery following initiation of a peer review process in which feedback of population incidence rates played a part. Blowers and Parker attribute temporal changes in tonsillectomy rate in a Vermont hospital service area in part to similar feedback. They also attribute change to the introduction of a process of consultation between pediatrician and surgeon to reach a joint decision on recommending tonsillectomy.¹⁰ A recent study on rate of elective surgery among union members shows that use of consultations can change surgery rates.¹¹ This evidence suggests that in the development of quality assurance programs, particular attention should be given to the value of a

second opinion (particularly from a member of a second specialty) in reducing geographic variations in use of medical care.


It must be recognized, however, that a fundamental reason for variations in incidence of surgery is uncertainty concerning the relationship between the use of a specific treatment and the health status of the receiving individuals. A large portion of common medical and surgical practices have not been rigorously evaluated prior to their widespread use. An excellent review of the extent of the problem of uncertainty concerning the effectiveness of conventional medical practices is provided by Cochrane.¹² The importance of reducing uncertainty concerning which level of use of procedures is appropriate can be justified on the basis of social costs alone. To provide every area in Maine with the nine procedures at the rate observed in the highest area would require an additional investment of ten million dollars. Use of procedures at the low rate means a saving of over six and one half million dollars — a sum which presumably could be invested in other health producing services; but since the costs and benefits of the procedures and their alternatives are commonly unknown, the health implications of the varying levels of resource use cannot be fully evaluated. Without such information, it is not possible to project accurately health care costs, or, indeed, to plan rationally for the development of health care systems which maximize the health of the population.

These considerations lead us to suggest that quality assurance programs seek to deal with the problem of geographic variations. In cases where variations cannot be attributed reasonably to differences in access of the population-at-risk to physician care, they should be interpreted as an indicator of the range of difference in professional opinion on use of specific technologies. Extensive review of the indications for the procedure and instigation of joint decision making by two or more physicians may lead to a lesser range of variation. But when professional disagreement on the nature of need or the value of a procedure persists, the disagreement should be openly recognized (as a necessary part of the art and science of medicine) and this recognition should lead to well designed studies to further resolve uncertainty. Such studies, we suggest, should become an integral part of a quality assurance program.

CONCLUSION

The incidence of total surgical discharges and nine common surgical procedures show extensive variation across neighboring Hospital Service Areas in the State of Maine. The pattern of variation and the findings of studies in other geographic areas sug-

Continued on Page 149



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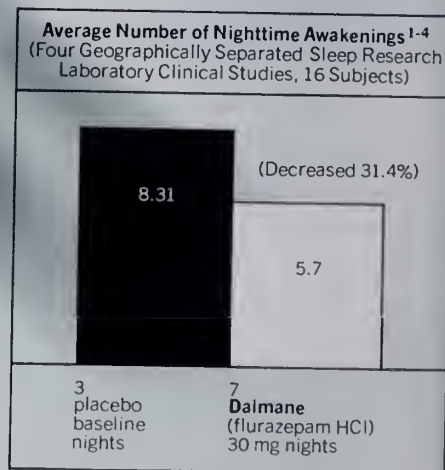
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REFERENCES:

1. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971
2. Frost JD Jr: A system for automatically analyzing sleep. Scientific exhibit at the 24th annual Clinical Convention of the American Medical Association, Boston, Nov 29-Dec 2, 1970; and at the 42nd annual scientific meeting of the Aerospace Medical Association, Houston, Apr 26-29, 1971
3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
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Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

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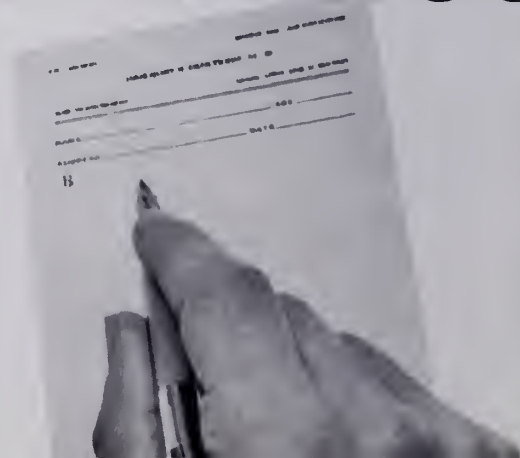
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Here are a few definitive statements in the O.T.A. report:

"...the problem of bioinequivalency in chemically equivalent products is a real one. Since the studies in which lack of bioequivalence was demonstrated involved marketed products that met current compendial standards, these documented instances constitute unequivocal evidence that neither the present standards for testing the finished product nor the specifications for materials, manufacturing process, and controls are adequate to ensure

that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.



"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and

(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or (c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription...



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*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

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Program – 122nd Annual Session

Maine Medical Association

June 14, 15, 16, 17, 1975

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Section on Ophthalmology of the M.M.A.

Maine Neurosurgical Society

Maine Psychiatric Association

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Maine Thoracic Society

For this cooperation and support, the members of the Scientific Committee are grateful.

Information

Registration:

Registration throughout the session will be in the Lobby at the Treadway-Samoset. Registration fee \$2.00.

Saturday, June 14 — 12:00 M. to 5:00 P.M.

Sunday, June 15 — 9:00 A.M. to 5:00 P.M.

Monday, June 16 — 9:00 A.M. to 6:00 P.M.

Tuesday, June 17 — 9:00 A.M. to 3:00 P.M.

Telephone: The number at the Treadway-Samoset is Rockport, (207) 594-2511.

Visiting Delegates:

Introduction of Visiting Delegates will take place at meetings of the House of Delegates on Saturday, June 14 and Sunday, June 15.

Technical Exhibits:

This year, twenty-five companies are contributing to the success of the annual session program by participating in the Technical Exhibits. A list of the exhibiting companies and representatives will be found on pages 136 and 137 of this program.

Please show your appreciation for the support of these companies by visiting these exhibits.

Badge Code:

Badges with green borders indicate Officers, Past Presidents, Delegates and Alternate Delegates of the M.M.A.; yellow borders, members of the M.M.A.; blue borders, guests; red borders, exhibitors; and plain white for the members of the Woman's Auxiliary.

Saturday, June 14

2:00 P.M. First Meeting of the House of Delegates

Call to Order: JOHN B. MADIGAN, M.D., President

Presiding: Speaker of the House, GEORGE W. BOSTWICK, M.D.

Presentation of the A. H. Robins' Physician Award for Community Service

Presentation of the Maine Blue Cross and Blue Shield "Award of Appreciation"

5:00 P.M. Tour of PenBay Medical Center

7:30 P.M. Dinner

Sunday, June 15

8:30 A.M. Reference Committee Meetings

12:30 P.M. Luncheon

2:00 P.M. Second Meeting of the House of Delegates

Election of President-elect, Executive Committee District Members and A.M.A. Delegate and Alternate

6:30 P.M. Treadway-Samoset Reception

7:30 P.M. Lobster Dinner

Monday, June 16

Scientific Program

9:30 A.M. to 12:30 P.M.

Welcome — BRADLEY E. BROWNLOW, M.D.

9:30 A.M. **Pediatric Urology**

ALAN B. RETIK, M.D., Associate in Surgery, Peter Bent Brigham Hospital and Children's Hospital Medical Center; Clinical Professor of Surgery (Urology), Tufts University Medical School and Chief of Pediatric Urology, Boston Floating Hospital for Infants and Children, Boston

10:30 A.M. **Methodology of Review of Quality Care**

DANIEL HAMATY, M.D., Assistant Clinical Professor, Yale University; Medical Director, Connecticut Medical Institute and Director, Pilot Project, ("Assessment by Performance"), American Society of Internal Medicine, Guilford, Connecticut

12:30 to 2:00 P.M. Luncheon

Scientific Program

2:00 to 4:00 P.M.

Welcome — GEORGE E. DAVIS, M.D.

Sponsored by the Maine Chapter, American College of Surgeons and the Maine Trauma Committee

Presiding — EDWARD K. MORSE, M.D., Rockland

2:00 P.M. **Emergency Medical Services**

DAVID R. BOYD, M.D.C.M., Director, Division of Emergency Medical Services, Department of Health, Education & Welfare, Bureau of Medical Services, West Hyattsville, Maryland

5:30 to 7:00 P.M. **Oysters and Keg Party** —

Sponsored by Marion Laboratories, Inc.

7:00 P.M. **Annual Banquet**

Presentation of Honorary Pins

President's Address: JOHN B. MADIGAN, M.D.

Tuesday, June 17

Scientific Program

9:30 A.M. to 12:30 P.M.

Welcome — BRADLEY E. BROWNLOW, M.D.

9:30 A.M. **Gallstones: Cause and Dissolve**

ELDON SHAFFER, M.D., F.R.C.P.(C), Department of Gastroenterology, Montreal General Hospital, Montreal

10:30 A.M. **Project HOPE**

WILLIAM B. WALSH, M.D., President, Project HOPE, Washington

12:30 to 2:00 P.M. Luncheon

Scientific Program

2:00 to 4:00 P.M.

Welcome — ROBERT H. PAWLE, M.D.

Sponsored by the Maine Medico-Legal Society

Presiding — GEORGE O. CHASE, M.D., President, Bangor

2:00 P.M. **Technical Aspects in the Use of the Iodine-Silver Plate Transfer Method**

MR. EDWARD CAMPBELL, Forensic Analyst, Latent Fingerprint Unit, Ontario Provincial Police, Toronto

3:00 P.M. **Iodine-Silver Plate Transfer Method of Recording Fingerprint Evidence**

MR. JOHN F. HINDS, Forensic Analyst in Charge, Fingerprint Identification Area, Ontario Provincial Police, Toronto

Specialty Group Meetings

Monday, June 16

1:30 P.M. MAINE SOCIETY OF INTERNAL MEDICINE AND THE AMERICAN COLLEGE OF PHYSICIANS

JOSEPH J. HIEBEL, M.D., Waterville and PHILIP P. THOMPSON, JR., M.D., Portland, presiding

Business Meeting

2:00 P.M.

Medical Records, Requirements, Confidentiality and Government Programs

CARMAULT B. JACKSON, JR., M.D., ASIM Trustee, San Antonio

The Federation of American Internists

TRUMAN G. SCHNABEL, JR., M.D., Immediate Past President of A.C.P., Philadelphia

2:00 P.M. SECTION ON OPHTHALMOLOGY OF THE M.M.A.

GARDNER N. MOULTON, M.D., Bangor, presiding

Whither Ophthalmology? — to be discussed by members of the Section on Ophthalmology

2:00 P.M. MAINE CHAPTER, AMERICAN ACADEMY OF PEDIATRICS

MAURICE ROSS, M.D., Saco, presiding

Optimism in the Identity Crisis

SPRAGUE W. HAZARD, M.D., Chairman, District I, American Academy of Pediatrics, Brandeis University Health Services, Waltham, Massachusetts

4:00 P.M. MAINE NEUROSURGICAL SOCIETY

DANIEL A. ROCK, M.D., Lewiston, President, presiding

Tuesday, June 17

8:30 A.M. MAINE PSYCHIATRIC ASSOCIATION

JOHN A. ORDWAY, M.D., Bangor, presiding

Council Meeting

11:00 A.M.

Meeting of Committees

2:00 P.M.

Continuing Education

HOWARD M. KERN, M.D., Director of Continuing

Education, American Psychiatric Association, Washington

11:00 A.M. MAINE RADIOLOGICAL SOCIETY

PETER E. GIUSTRA, M.D., Rockland, presiding

Executive Committee Meeting

2:00 P.M. Meeting

2:00 P.M. MAINE SECTION, AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS

ROBERT M. KNOWLES, M.D., Portland, presiding

Annual Maine Section Meeting of ACOG

ROBERT M. KNOWLES, M.D., Section Chairman of the American College of Obstetrics and Gynecology, Portland

2:00 P.M. MAINE THORACIC SOCIETY

GISELA K. DAVIDSON, M.D., Portland, presiding

New Concepts in the Diagnosis and Management of Pulmonary Embolism

ARTHUR A. SASAHARA, M.D., Chief, Medical Service, V.A. Hospital, West Roxbury, Massachusetts and Professor of Medicine, Harvard Medical School

SPECIAL NOTICES

Executive Committee Meetings

The Executive Committee will meet on Saturday, June 14 and daily throughout the session at a time and place to be announced.

Informal Luncheons

Maine Academy of Orthopedic Surgeons — Monday, June 16.

Maine Psychiatric Association — Tuesday, June 17.

Breakfast Meeting

Committee on Medicine and Religion — Monday, 8:00 A.M.

SPEAKER: A. MARSHALL SMITH, M.D., Chief of Pulmonary Medicine, Eastern Maine Medical Center, Bangor

SUBJECT: Spiritual Values in the Care of Pulmonary Disease

Honorary Pins

Presentation of the Association's Honorary Pins will be made by John B. Madigan, M.D., President of the M.M.A., at the Annual Banquet, Monday evening, June 16 at 7:00 P.M.

FIFTY-YEAR PINS

Fifty-Year Pins will be presented to the following members who were graduated from Medical School in 1925.

Cumberland County

John J. Lappin, M.D.

New York University School of Medicine

Philip H. McCrum, M.D.

Harvard Medical School

Alice A. S. Whittier, M.D.

Yale University School of Medicine

FIFTY-FIVE-YEAR PINS

Fifty-Five-Year Pins will be presented to the following members who were graduated from Medical School in 1920.

Cumberland County

Winifred W. Curtis, M.D.

Boston University School of Medicine

Isaac M. Webber, M.D.

Bowdoin Medical School

Kennebec County

Blynn O. Goodrich, M.D.

McGill University Faculty of Medicine

Ella Langer, M.D.

University of Vienna Medical College

Knox County

George Loewenstein, M.D.

Friedrich Wilhelms University, Germany

Oxford County

James A. MacDougall, M.D.

McGill University Faculty of Medicine

SIXTY-YEAR PINS

Sixty-Year Pins will be presented to the following members who were graduated from Medical School in 1915.

Cumberland County

Elton R. Blaisdell, M.D.

Bowdoin Medical School

Kennebec County

Albert S. Crawford, M.D.

Cornell University College of Medicine

York County

Charles W. Kinghorn, M.D.

Bowdoin Medical School

Harold W. Stevens, M.D.

Harvard Medical School

SIXTY-FIVE-YEAR PIN

A Sixty-Five-Year Pin will be presented to the following member who graduated from Medical School in 1910.

Penobscot County

Thomas A. Devan, M.D.

Johns Hopkins University Medical College

SEVENTY-YEAR PIN

A Seventy-Year Pin will be presented to the following member who graduated from Medical School in 1905.

Androscoggin County

Daniel F. D. Russell, M.D.

Bowdoin Medical School

26th Annual Meeting

Woman's Auxiliary

to the

Maine Medical Association

Open to all Physicians' Wives

Sunday, June 15

9:00 A.M. to 12:00 M. Registration

Lobby, Treadway-Samoset, Rockport

9:30 to 10:15 A.M. Open House Coffee for M.D.'s Wives

The Library

Hostess: MRS. RICHARD TAYLOR

10:15 to 11:30 A.M. House of Delegates Annual Business Meeting — Installation

The Library

MRS. ROBERT F. FICKER, President, presiding

11:30 A.M. to 12:00 M. "MMA COMES TO WAMMA"

12:00 to 12:30 P.M. Reception Honoring Members-at-Large and M.M.A. Executive Committee members

The North Samoset Room

12:30 P.M. Annual Luncheon

The North Samoset Room

Hostesses: Members-at-Large, newly organized

Lincoln-Sagadahoc Auxiliary

MRS. ROBERT F. FICKER, presiding

Welcome — MRS. JAMES SMITH, Annual Meeting Chairman

Lord's Prayer — MR. KEVIN BROWN

Invocation — FATHER LEO J. GOUDREAU

Forecast — EUCLID M. HANBURY, JR., M.D., President-elect M.M.A.

Guest Speaker — CLEMENT A. HIEBERT, M.D.,
Portland

2:00 P.M. Adjournment

2:15 P.M. 1975-1976 Board of Directors Meeting
The Library

Visiting Delegates

The Connecticut State Medical Society
NORMAN H. GARDNER, M.D., East Hampton
BERNARD O. NEMOITIN, M.D., Stamford

New Hampshire Medical Society
FRANK KENNEDY, II, M.D., Exeter

The Rhode Island Medical Society
RUSSELL HAGER, M.D., Warwick

Vermont State Medical Society
HARRY M. ROWE, M.D., Wells River

Delegates to Out-of-State Meetings

The Connecticut State Medical Society
RICHARD M. SWENGEL, M.D., Lewiston

The Massachusetts Medical Society
EUCLID M. HANBURY, JR., M.D., Belfast

New Hampshire and Vermont State Medical Societies
DONALD L. ANDERSON, M.D., Lewiston

Medical Society of the State of New York
ROBERT F. FICKER, M.D., Kennebunkport

The Rhode Island Medical Society
LEONARD G. MIRAGLIUOLO, M.D., Bangor

"Medicine Avenue"

Technical Exhibits

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60064

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and Bruce Reynolds

Ayerst Laboratories, 685 Third Ave., New
York, New York 10017

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Bristol Laboratories, P.O. Box 657, Syracuse,
New York 13201

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search Triangle Park, North Carolina 27709

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Sheafe St., Portsmouth, New Hampshire 03801

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County Delegates

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Paul A. Brinkman, M.D.	Paul E. Floyd, M.D.
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Terrance J. Sheehan, M.D.	Charles E. Towne, M.D.

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Pharmacotherapy of Essential Hypertension

DAVID W. DUHME, M.D., DAVID J. GREENBLATT, M.D. and
RUSSELL R. MILLER, Pharm.D., Ph.D.

Hypertension affects 10 to 20% of the adult population and is a major risk factor in the development of cerebrovascular disease, congestive heart failure, myocardial infarction, and renal insufficiency.¹⁻¹¹ Since pharmacotherapy of essential hypertension reduces the likelihood of these complications, detection and treatment of this disease is a public health problem of primary importance. This article will discuss some practical clinical aspects of the evaluation and treatment of hypertension.

DIAGNOSIS

It is important to distinguish between "hypertension" as an abnormal elevation of systemic arterial blood pressure measured by sphygmomanometer and stethoscope, and "hypertension" as a complex disease state. All individuals experience minute-to-minute and day-to-day fluctuations in arterial blood pressure, occasionally into the "hypertensive" range. Accordingly, the presence or absence of hypertension, the disease, must be diagnosed on an individual basis, evaluating at least three and preferably more blood pressure measurements, and looking for signs of end-organ damage in the retina or heart. The likelihood that hypertensive disease is present in a given patient increases with the frequency of hypertensive readings on repeated mea-

surement. Conversely, an individual is likely to be "normotensive" if the frequency of normal blood pressure readings on repeated measurement is high. Patients in whom no consistent pattern of "hypertensive" or "normotensive" blood pressure is observed (i.e., those with "labile" hypertension) present a diagnostic and therapeutic enigma. They should be followed at least annually for the development of "sustained" hypertension.¹²

The levels of blood pressure that divide "normotensive" from "hypertensive" are controversial, arbitrary, and not always clinically satisfactory. Epidemiologic studies suggest that a systolic blood pressure consistently in excess of 140 mmHg and/or a diastolic pressure consistently in excess of 90 mmHg constitutes clinically important hypertension with the associated risks of cerebrovascular, cardiac, and renal disease.¹⁻¹¹ The risk of these complications further increases at higher levels of sustained blood pressure. Pharmacologic reduction of blood pressure partially or completely nullifies these risks. Most hypertensive patients have elevations in both systolic and diastolic blood pressure, but some have only "isolated" systolic hypertension (i.e., 180/80 mmHg). This is commonly encountered in elderly individuals with reduced compliance (stiffening) of the aorta and larger arteries due to atherosclerotic vascular disease.¹³ Predictably, such individuals have a high incidence of cerebrovascular disease, but the evidence that treatment of blood pressure reduces the risk is not very convincing.

EVALUATION

Table 1 lists a variety of diagnostic tests used to evaluate specific causes and consequences of hypertension. They range from those that should be performed in most or all patients to those that are appropriate only in very selected cases. The diagnostic work-up should be individualized; no fixed scheme or protocol can be considered rational. The extent of evaluation depends upon the patient's age, family history of essential hypertension, and severity of disease. It is reasonable to reopen the search for curable causes at a later date if a patient's blood pressure proves difficult to control. The physician must weigh the cost, discomfort, and hazard of each

David W. Duhme, M.D. is a practicing physician at the Brookside Park Family Life Center, 49 Brookside Avenue, Jamaica Plain, Boston 02130; and a former Clinical Fellow in Medicine and Pharmacology, Massachusetts General Hospital and Harvard Medical School.

David J. Greenblatt, M.D. is Assistant in Medicine, Clinical Pharmacology Unit, Massachusetts General Hospital, Boston 02114; and Assistant Professor of Medicine (Clinical Pharmacology), Harvard Medical School.

Russell R. Miller, Pharm.D., Ph.D. is Director of Clinical Programs, Department of Pharmacy, New England Medical Center Hospital, Boston 02111; Assistant Professor of Pharmacology, Boston University School of Medicine; and Adjunct Associate Clinical Professor of Pharmacy, Massachusetts College of Pharmacy.

Drug Therapy Reviews is supported by the Bingham Associates Fund through a grant-in-aid to the "Focus on Pharmacy" program, a joint project of the Departments of Pharmacy of the Maine Medical Center, Portland, and the New England Medical Center Hospital, Boston.

Address reprints to Dr. Miller at Box 420, New England Medical Center Hospital, Boston, MA 02111.

TABLE 1

EVALUATION OF THE HYPERTENSIVE PATIENT

Most or All Patients Should Have:

Medical history
Physical examination
Blood urea nitrogen or creatinine determination
Serum sodium, potassium, chloride, and bicarbonate determinations
Electrocardiogram*
Chest x-ray*
Urinalysis

Selected Patients Should Have: If There is Reason to Suspect:

Urine culture	Chronic pyelonephritis
Intravenous pyelogram	Urinary tract obstruction, renovascular disease, or renal parenchymal disease
24-hour excretion of vanillyl-mandelic acid (VMA)	Pheochromocytoma
Creatinine clearance	Renal insufficiency
Plasma renin activity	High- or low-renin hypertension
Serum thyroxine determination	Thyrotoxicosis
Serum cortisol determination	Cushing's syndrome
Furosemide-stimulated upright plasma renin activity	Low-renin essential hypertension or primary aldosteronism

*Very Selected Patients Can Have:**If There is Reason to Suspect:*

Bilateral renal vein renin determination	Renovascular disease
Renal arteriography	Renovascular disease or neoplasm
Aldosterone excretion rate	Primary aldosteronism
Tyramine stimulation test	Pheochromocytoma
Dexamethasone suppression test	Cushing's syndrome

* in patients aged 40 or over

diagnostic test against the likelihood that it will reveal something of clinical or therapeutic importance.

"Curable" causes of hypertension (Table 2) are unusual.¹⁴⁻¹⁸ Aspects of the clinical history (i.e., episodic sweating or palpitations), physical examination (i.e., Cushingoid features, abdominal bruits, decreased femoral pulses, signs of hyperthyroidism), or laboratory data (i.e., hypokalemia, elevated plasma renin activity, rib notching on chest x-ray) may suggest that one of these diseases is present, and lead to further diagnostic evaluation (Table 1). In more than 95% of cases, however, no curable underlying disease will be found, and the diagnosis of "essential" hypertension will be assigned. Essential hypertension typically is a familial disease, of asymptomatic and insidious onset between ages 30 and 50 years, and gradually progressive. It is characterized by normal cardiac output, increased

TABLE 2

"CURABLE" CAUSES OF HYPERTENSION

Pheochromocytoma
Renovascular disease
Renal parenchymal disease
Primary aldosteronism
Coarctation of the aorta
Urinary tract obstruction
Cushing's syndrome
Thyrotoxicosis
Hypertension of pregnancy
Pharmacologically-induced hypertension

peripheral vascular resistance, and normal values of extracellular fluid volume, plasma renin activity, aldosterone secretion, and plasma catecholamines. The pathophysiology of essential hypertension is exhaustively reviewed elsewhere.^{11,13,19-28}

TREATMENT OF ESSENTIAL HYPERTENSION

Most diagnosed hypertensive patients are untreated or inadequately treated. Physicians are partly to blame for this unfortunate situation. Many clinicians still believe that essential hypertension is a "benign" disease that does not need vigorous therapy. Others are unfamiliar with the pharmacology of antihypertensive drugs and are unable to select an effective combination of drugs. Poor patient compliance is also a major contributor to apparent failure of treatment. Patients are understandably unwilling to accept the need for lifelong drug therapy of an asymptomatic disease, particularly when the drugs are expensive and may produce troublesome side effects.²⁹ Physicians must intensify their commitment to identifying and effectively treating hypertension. The general public and patients in particular must be educated as to the asymptomatic nature of hypertension,³⁰ its high morbidity and mortality when untreated, its excellent response to medical therapy, and the fact that therapy must be lifelong. Nonphysician specialists — including pharmacists, nurse practitioners, dentists and physician's assistants — can play an important role in education and in antihypertensive drug therapy.³¹ The increased availability of such specialists will contribute greatly to the management of this public health menace.

DIURETICS

Thiazide diuretics are the cornerstone of antihypertensive drug therapy. Most, if not all, hypertensive patients should receive a thiazide as the initial mode of therapy.^{11,13,32,33} The hypotensive action of these drugs is not fully explained by their ability to deplete the body of sodium and water; thiazides appear to lower peripheral vascular resistance by a mechanism which is not well understood.³⁴⁻³⁶ All thiazide diuretics are clinically equivalent except for variations in milligram potency. Pharmaceutical

APPENDIX 1

DOSAGE AND WHOLESALE COST OF ANTIHYPERTENSIVE AGENTS

<i>Generic Name</i>	<i>Trade Name(s)</i>	<i>Range of Usual Daily Doses (mg)</i>	<i>Oral Dosage Sizes Available (mg)</i>	<i>Cost per 100 dose units^b</i>
THIAZIDE DIURETICS				
Chlorothiazide	Diuril	500-1000	250 500	3.23 5.10
Hydrochlorothiazide	Hydrodiuril, Esidrix, Oretic, ^a Thiuretic ^a	50-100	25 50	3.08-3.80 4.84-6.00
Benzthiazide	Aquapres, Aquatag, Diucen, Edemex, Exna, Lemazide, ^a Proqua, Hy-Drine	50-100	25 50	3.20-3.80 5.00-6.25
Hydroflumethiazide	Saluron, Diucardin ^a	50-100	50	3.88-5.26
Bendroflumethiazide	Naturetin	5-10	2.5 5.0 10	4.52 7.15 11.53
Cyclothiazide	Anhydron	2-4	2	6.04
Methyclothiazide	Aquatensen, Enduron ^a	5-10	2.5 5.0	4.84 6.56-6.88
Trichlormethiazide	Naqua, Metahydrin ^a	4-8	2 4	2.82-3.37 4.44-5.25
Polythiazide	Renese	2-8	1 2 4	4.29 6.78 11.30
POTASSIUM-SPARING DIURETICS				
Triamterine	Dyrenium	100-200	100	6.85
Spironolactone	Aldactone	50-400	25	9.75
OTHER DIURETICS				
Furosemide	Lasix	20-80	20 40	6.00 8.40
Ethacrynic acid	Edecrin	25-100	25 50	4.58 6.54
Chlorthalidone	Hygroton	50-100	50 100	7.32 8.88
Quinethazone	Hydromox	50-100	50	6.36
Metolazone	Zaroxolyn	5-10	2.5 5 10	6.47 7.65 8.82
DIURETIC COMBINATIONS				
Hydrochlorothiazide (25 mg) plus Triamterine (50 mg)	Dyazide	1-4 capsules		7.15
Hydrochlorothiazide (25 mg) plus Spironolactone (25 mg)	Aldactazide	2-8 tablets		10.97
RAUWOLFIA ALKALOIDS				
Whole Root Rauwolfia	Hyper-Rauw, ^a Raudixin, Rauval, ^a Wolfina, Serfolia, Serfia ^a (generic)	50-100	50 100 50 100	1.35-3.97 1.75-6.62 0.55 ^c 0.70 ^c
Alseroxylon	Rautensin, ^a Rauwiloid	2-4	2	6.77-6.88
Deserpidine	HarmonyI	0.1-0.25	0.1 0.25	2.84 4.77
Rescinnamine	Moderil	0.25-0.5	0.25 0.5	4.22 5.91
Syrosingopine	Singoserp	1-2	1	4.65

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Reserpine	Elserpine, Lemiserp, Rau-Sed, Resercent, Reserpoid, Sandril, ^a Serpasil, Serpate, Vio-Serpine, Raurine, Serpanray (generic)	0.1-0.25	0.1	0.63-4.05
			0.25	1.05-9.12
			0.1	0.40 ^c
			0.25	0.45 ^c
OTHER SYMPATHOPLÉGIC AGENTS				
Methyldopa	Aldomet	500-2000	250	6.36
			500	11.45
Clonidine	Catapres	0.2-0.8	0.1	5.95
			0.2	7.80
Guanethidine	Ismelin	10-300	10	8.40
			25	11.75
VASODILATORS				
Hydralazine	Apresoline	40-200	10	2.60
			25	3.85
			50	5.15
			100	7.20
	Lopress ^a		10	1.45
			50	3.75
	(generic)		10	0.95 ^c
			25	1.29 ^c
BETA-ADRENERGIC ANTAGONISTS				
Propranolol	Inderal	30-320	10	3.66
			40	6.18

^a—indicates the least expensive brand name product among those available

^b—when more than one brand name product is available the range of prices is specified

^c—indicates the lowest price among generic products available

claims notwithstanding, differences in pharmacologic half-life and duration of diuretic action are not clinically important. In fact, all thiazides continue to exert an antihypertensive effect long after they have been eliminated from the body. Chlorthalidone is equivalent to thiazides in clinical action, but is more expensive. In clinical practice, the least expensive thiazide derivative should be prescribed (Appendix 1). Doses equivalent to 1.0 gm of chlorothiazide should be administered once daily or in two divided doses.

All patients on chronic thiazide therapy undergo a depletion of total body potassium content,^{37,38} although only about one-third of patients reach our arbitrarily-defined "hypokalemic" level of serum potassium concentration.³⁹ Hypokalemia should not be permitted to develop in any patient receiving concurrent therapy with digitalis glycosides. In other patients, however, there is no good evidence that moderate potassium depletion is harmful.⁴⁰ Only rarely does hypokalemia produce symptoms. Many patients tolerate concentrations of less than 3.0 mEq/liter for years without apparent ill effects. Difficult as it is for physicians to ignore drug-

induced abnormalities in laboratory tests, the need for prophylactic or corrective potassium in asymptomatic thiazide recipients is not established. The same can be said for other metabolic abnormalities induced by thiazides.⁴¹⁻⁴³ Hyperuricemia need not be treated unless very high serum urate concentrations (i.e., greater than 12 mg/100 ml) are reached or clinical gout occurs. Hyperglycemia can be tolerated as long as it remains asymptomatic or, in patients with pre-existing diabetes, clinical control is not disrupted.

In patients who cannot tolerate thiazides, a "potassium-retaining" diuretic can be substituted. Spironolactone (100 mg per day) and triamterene (100 to 200 mg per day) differ from each other in structure and pharmacologic mechanism of action but are clinically very similar.⁴⁴ Either drug can be used instead of thiazides, or together with thiazides to prevent potassium loss and possibly to potentiate their hypotensive effect.⁴⁵⁻⁴⁸ Unfortunately, many male patients develop gynecomastia during long-term spironolactone therapy.⁴⁹⁻⁵¹ Potassium-retaining diuretics should not be coadministered with potassium chloride and should be given with great

caution when renal insufficiency is present.⁵²

Furosemide is commonly administered for anti-hypertensive therapy,⁵³⁻⁵⁴ but it is no more effective than thiazides and can produce excessive diuresis.^{55,56} Furosemide should be used only when fluid retention or edema occurs with other diuretics.

ADJUNCTIVE THERAPY

For many hypertensive patients a thiazide alone will reduce blood pressure satisfactorily. If three to six weeks of thiazide treatment is not adequately hypotensive, then a second drug should be initiated. A variety of "tracks" are possible, but all forms of adjunctive therapy produce retention of salt and water which can partially or completely nullify the hypotensive effect of these drugs.⁵⁷⁻⁵⁹ Therefore, diuretics *must* be continued and coadministered with all other forms of antihypertensive therapy.

Sympathoplegia

Methyldopa, reserpine, and guanethidine are familiar antihypertensive agents.^{59,60} Each drug interferes with adrenergic nervous system function, and each has important side effects. These three drugs are traditional and time-tested hypotensive agents, but probably will become relegated to a secondary role as the advantages of other forms of therapy become understood by practicing physicians.

Methyldopa reduces blood pressure by poorly understood mechanisms, with its predominant effect in the central nervous system.^{59,62} Usual effective doses of methyldopa range from 0.5 to 2.0 gm per day, traditionally given in two to four divided doses. Unfortunately, methyldopa commonly produces dose-dependent drowsiness and somnolence.^{63,64} The consequences of this can be minimized by giving a larger quantity at bedtime. In patients requiring relatively low doses, for example, a single bedtime dose of 0.5 to 0.75 gm may be appropriate.⁶⁵ Mild postural hypotension and nasal congestion are other common side effects of methyldopa.^{59,63} Sexual dysfunction and Coombs-positive hemolytic anemia⁶⁶⁻⁶⁹ are relatively uncommon. Jaundice and hepatic necrosis, fortunately, are rare.⁷⁰⁻⁷⁵ *Clonidine*, a newly-released antihypertensive agent, appears to resemble methyldopa in its action.⁷⁶⁻⁸⁰ The role of clonidine in clinical practice is not yet established.

Reserpine and its congeners deplete catecholamine neurotransmitters from the brain and from the peripheral sympathetic nervous system.^{59,81,82} Oral reserpine has a mild antihypertensive effect which in most patients is less powerful than methyldopa. Usual effective doses are 0.1 to 0.25 mg given once daily. Depression is the most important of many central nervous system side effects induced by reserpine; suicide apparently has resulted in some

cases.⁸³⁻⁸⁵ Nasal congestion and excessive salivation are less serious but troublesome side effects. Reserpine stimulates gastric acid secretion and might produce or exacerbate peptic ulcer disease.^{86,87} The recent findings that reserpine may be associated with breast cancer in females is of considerable concern.⁸⁸⁻⁹⁰ Reserpine use should be restricted to situations in which once-a-day dosage and low cost are essential for an individual patient.

Guanethidine appropriately is relegated to the status of a "last-ditch" agent, reserved for clinical situations in which other sympathoplegic agents fail. Guanethidine prevents the uptake and storage of norepinephrine in presynaptic nerve terminals and produces a dose-dependent partial or complete sympathetic blockade.⁹¹⁻⁹³ Effective doses are variable, ranging from 10 mg to 300 mg or more per day. The antihypertensive effect of guanethidine must be carefully titrated, with the patient's blood pressure measured in the sitting and standing positions. Guanethidine has a slow onset and long duration of action; dosage adjustments should be made no more often than once every 5 days.

Essentially all patients taking effective doses of guanethidine experience side effects. The most common are postural hypotension, impairment of male sexual function, and diarrhea.^{63,94,95} In fact, the clinical efficacy and value of guanethidine in a given patient usually depends upon his or her ability to adjust to and live with the inevitable side effects that accompany effective doses. Sometimes the required dose of guanethidine can be reduced by coadministration of 1.0 gm per day of methyldopa. On the other hand, the antihypertensive effect of guanethidine is nullified by coadministration of tricyclic antidepressants or phenothiazines;^{96,99} such drug combinations should be avoided. Guanethidine can cause paradoxical hypertension in patients with pheochromocytoma, and is contraindicated in this disease.

Peripheral Vasodilation and Beta-Blockade

Antihypertensive therapy with vasodilating drugs and beta-adrenergic blocking agents, alone or in combination, is a second major approach to adjunctive antihypertensive therapy. Treatment with such drugs is often more effective than with sympathoplegic agents and invariably better tolerated by patients. Important drawbacks include the need for multiple daily dosage and the lack of federal sanction for the use of propranolol as an antihypertensive agent.

Hydralazine reduces blood pressure by producing relaxation of resistance arterioles.¹⁰⁰ A consequence of this action is compensatory reflex sympathetic stimulation resulting in tachycardia, palpitations, and increased cardiac work. Hydralazine given alone therefore can exacerbate angina in pa-

tients with ischemic heart disease. The reflex effects of hydralazine are prevented by coadministration of propranolol, and the two drugs should be used in combination in all but the youngest patients. A typical initial dose of hydralazine is 10 mg 4 times daily, which can be gradually increased to as much as 50 mg 4 times daily. Higher doses should be administered with caution, since these doses can induce an autoimmune syndrome resembling lupus erythematosus (LE). The syndrome is characterized by appearance of antinuclear antibodies (ANA) and "LE cells" in the blood, as well as symptoms such as fever and arthralgia.^{101,102} Hydralazine-induced LE is more common at high daily doses and during prolonged administration.¹⁰³ Patients on chronic hydralazine therapy should have periodic checks of ANA titer, although a rise in titer without accompanying symptoms does not necessarily require drug discontinuation.

Propranolol is the only beta-adrenergic antagonist available for clinical use in the United States. It is an effective antihypertensive agent when given in combination with a diuretic.¹⁰⁴⁻¹⁰⁷ Depression of cardiac output partially accounts for this action.^{107,108} It also appears that propranolol's ability to impair the release of renin by the kidney adds to the antihypertensive effect,¹³ although other beta-blockers which do not suppress renin activity are also antihypertensive.¹⁰⁹⁻¹¹¹ The use of propranolol as an antihypertensive agent is well-tolerated by patients because orthostatic blood pressure regulation and sexual function are not impaired. The usual initial dose of propranolol is 10 mg 4 times daily, which can be gradually increased to 40 mg 4 times daily or higher. Despite dozens of studies which document the safety and efficacy of propranolol as an antihypertensive agent,¹⁰⁴ the drug is not yet approved for the treatment of hypertension by the Food and Drug Administration.

The hazards and side effects of propranolol are reviewed in detail elsewhere.¹¹²⁻¹¹⁴ In healthy ambulatory patients, serious side effects are very unusual. Some individuals experience vague disturbances of gastrointestinal or central nervous system function, but these usually do not necessitate discontinuation of the drug. Propranolol should not be administered to patients with organic heart disease whose cardiac compensation depends upon beta-adrenergic stimulation of the heart; in such individuals small doses can rapidly produce catastrophic cardiovascular collapse. Propranolol is contraindicated in patients with asthma or other diseases associated with bronchospasm, and should be used with great caution in individuals with insulin-dependent diabetes mellitus.

TREATMENT OF LESS COMMON FORMS OF ESSENTIAL HYPERTENSION

Some forms of essential hypertension fall into

distinct subcategories. Patient management is possible without knowledge of these categories. Some physicians, however, find that characterization of individual cases enhances their understanding of the disease process and suggests the most rational approach to therapy. Characterization of essential hypertension involves the routine analysis of plasma renin activity with the patient taking no medications. Plasma renin activity determinations are not available to most physicians. Furthermore, certain subcategories of essential hypertension are most rationally treated with propranolol as a first-line drug. As mentioned previously, this use of propranolol is not approved by the Food and Drug Administration.

High-Output Hypertension

In some individuals hypertension is characterized by normal peripheral vascular resistance and high cardiac output.^{115,116} The syndrome is probably related or identical to the condition described as the "hyperdynamic beta-adrenergic circulatory state."¹¹⁷ Afflicted individuals tend to be young and to have episodic ("labile") hypertension, particularly systolic. It is sometimes associated with high levels of plasma renin activity. High-output labile hypertension may be a precursor of "sustained" essential hypertension with normal cardiac output.¹²

Propranolol is the most logical treatment for this form of hypertension,^{13,118,119} although the need for treatment is not clearly established. If fluid retention or compensatory increases in peripheral vascular resistance occur, a diuretic can be added.

High-Renin Hypertension

Essential hypertension can be associated with abnormally high plasma renin activity.¹³ Appropriately, the presence of renovascular disease often is suspected and evaluated in such patients, but usually is not found.

Propranolol is the initial drug of choice in these patients.¹³ For many, it is the only therapy required. However, if propranolol alone does not provide adequate control, a diuretic and a vasodilator should be added in that order.

*Low-Renin Hypertension*¹²⁰⁻¹²³

The association of hypertension with abnormally low levels of plasma renin activity — even after stimulation with a diuretic such as furosemide — suggests the presence of a mineralocorticoid-secreting tumor. Work-up of these patients seldom reveals such a tumor; aldosterone secretion and excretion rates are usually normal. Spironolactone (100 to 400 mg per day) is very effective in patients with low-renin hypertension,¹²⁴⁻¹²⁸ but long-term spironolactone therapy, particularly at high doses,

commonly results in unacceptable endocrine side effects.^{51,125,129} Thiazide diuretics appear to be equally useful,^{130,131} consistent with the observation that low-renin hypertensive patients have increased plasma volume and total body sodium content.

OTHER FORMS OF ANTIHYPERTENSIVE THERAPY

Salt Restriction

Hypertensive patients are traditionally told to reduce their salt intake. In fact, a reduction in blood pressure occurs only when sodium intake is curtailed to drastically low levels of 500 mg per day or less. Few patients will tolerate this. The availability of diuretics greatly reduces the need for dietary sodium restriction. A normal daily sodium intake of 4 to 6 gm probably has no influence on blood pressure control in an adequately-treated patient. However, it is reasonable to encourage patients to avoid excessive salt intake.

Sedative-Hypnotics

Regrettably many physicians administer sedative or antianxiety agents as the first approach to essential hypertension. Such drugs have no specific antihypertensive effect, and usually result in a sleepy but still hypertensive patient. Antianxiety agents may be used adjunctively with appropriate antihypertensive agents if anxiety is judged to play a significant role in the patient's disease. A non-enzyme-inducing drug such as a benzodiazepine derivative should be prescribed if antianxiety drug therapy is considered appropriate.¹³² Barbiturates such as phenobarbital stimulate microsomal enzymes and can potentially accelerate the metabolism of certain antihypertensive agents and reduce their clinical effect.^{133,134}

Monoamine Oxidase Inhibitors

Monoamine oxidase inhibitor drugs such as pargyline have been used as antihypertensive agents.¹¹ Although effective, the potential hazards and toxic effects of these drugs are unacceptable. Monoamine oxidase inhibitors have no place in modern antihypertensive drug therapy.

FIXED COMBINATION OF ANTIHYPERTENSIVE DRUGS

Numerous fixed combinations of two or more antihypertensive agents are available for clinical use (Appendix 2). Multiple drug therapy of essential hypertension can be rational and reasonable, but only when the dosage of each agent is carefully titrated to meet the needs of each patient. With fixed drug combinations, adjustment of dosage of one component alone is impossible. The use of such combinations is seldom rational except when the components of a particular preparation happen to

Continued on Page 145



Pro-Banthine®

brand of
propantheline bromide

Indications: Pro-Banthine is effective as adjunctive therapy in the treatment of peptic ulcer. Dosage must be adjusted to the individual.

Contraindications: Glaucoma, obstructive disease of the gastrointestinal tract, obstructive uropathy, intestinal atony, toxic megacolon, hiatal hernia associated with reflux esophagitis, or unstable cardiovascular adjustment in acute hemorrhage.

Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

Overdosage may cause a curare-like action, with loss of voluntary muscle control. For such patients prompt and continuing artificial respiration should be applied until the drug effect has been exhausted. Diarrhea in an ileostomy patient may indicate obstruction, and this possibility should be considered before administering Pro-Banthine.

Precautions: Since varying degrees of urinary hesitancy may be evidenced by elderly males with prostatic hypertrophy, such patients should be advised to micturate at the time of taking the medication.

Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

How Supplied: Pro-Banthine is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

SEARLE

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San Juan, Puerto Rico 00936

Address medical inquiries to: G. D. Searle & Co.
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"Antiacid" action for ulcer patients...

one of the many things you need in an anticholinergic.



Pro-Banthine is considered adjunctive in total peptic ulcer therapy that may include diet, conventional antacids, bed rest, and other supportive measures.

Pro-Banthine is provided in several different dosage forms which will meet virtually any clinical need. It is just as versatile in filling patient needs, among which are:

"Antiacid" action—Pro-Banthine® (propantheline bromide) reduces gastric secretory volume and resting total and free acid.

"Analgesic" action—Pro-Banthine helps to control the acid-spasm-pain complex.

Vigorous anticholinergic action—Pro-Banthine® Vials, 30 mg., are for intramuscular or intravenous use when prompt and vigorous anticholinergic action is required.

Mild anticholinergic action—Pro-Banthine® Half Strength, 7.5 mg. tablets, for more exact adjustment of maintenance dosage in mild to moderate gastrointestinal disorders.

Pro-Banthine® (propantheline bromide)

a good
option
in peptic
ulcer

in most cases of
sustained moderate hypertension,
ALDOMET[®] (METHYLDOPA|MSD)
usually offers more
than effective lowering
of blood pressure...



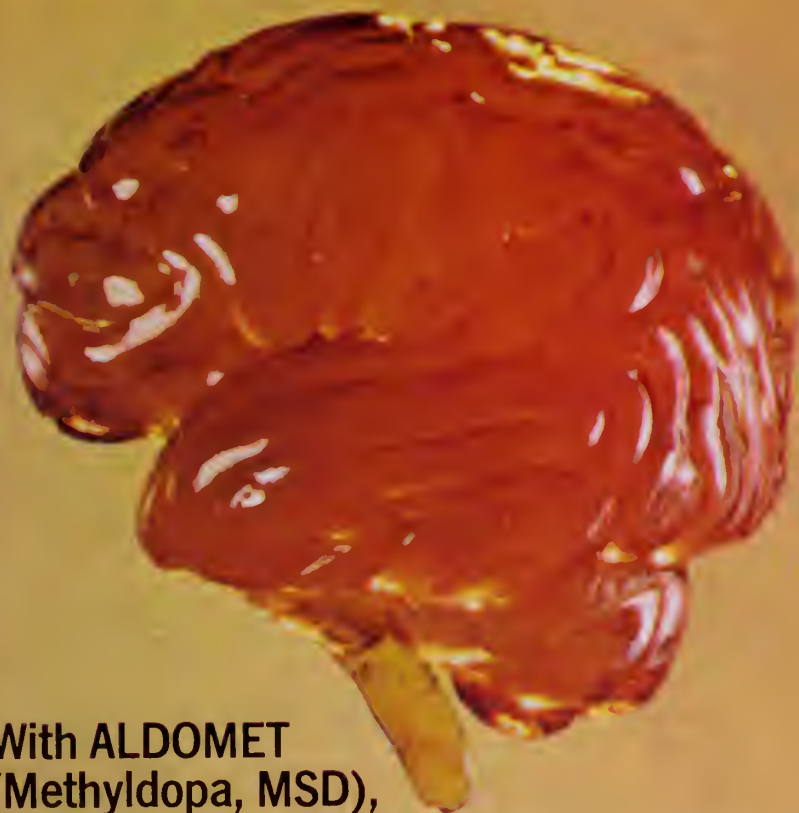
**With ALDOMET
(Methyldopa, MSD),
existing renal function
is usually unchanged**

ALDOMET has no direct effect on renal function. When used in effective doses, ALDOMET usually does not reduce glomerular filtration rate, renal blood flow, or filtration fraction.



**With ALDOMET
(Methyldopa, MSD),
cardiac output is
generally unchanged**

ALDOMET has no direct effect on cardiac function. When ALDOMET is used in effective doses cardiac output is usually maintained with no cardiac acceleration; in some patients the heart rate is slowed.



**With ALDOMET
(Methyldopa, MSD),
symptomatic postural
hypotension is infrequent**

ALDOMET reduces both supine and standing blood pressure. Less frequent symptomatic postural hypotension is experienced with ALDOMET than with many other antihypertensive agents. Exercise hypotension and diurnal blood pressure variations rarely occur.

**for sustained
moderate hypertension**

TABLETS, 250 mg and 500 mg

ALDOMET[®]
(METHYLDOPA|MSD)

a unique antihypertensive agent

Contraindications include active hepatic disease and known sensitivity to the drug. Use with caution in patients with a history of liver disease or dysfunction. Not recommended in pheochromocytoma or pregnancy.

It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

For a brief summary of prescribing information, please see following page.



to further
simplify therapy
for many patients

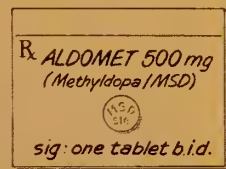
now available
ALDOMET[®] 500 mg
(METHYLDOPA | MSD)

- often more practical to prescribe
- easier for patients to remember

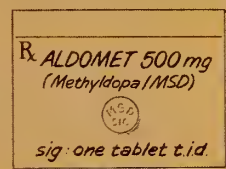
Now offered in addition to the standard 250-mg tablet, the new ALDOMET 500 mg tablet is a patient convenience. An especially important one, since in hypertension convenience of the dosage schedule is one factor that can make the difference in compliance of the patient. The minimum daily dose of ALDOMET is 250 mg b.i.d. The usual starting dose is 250 mg t.i.d. Dosage is adjusted as necessary by adding or deleting 250 mg or 500 mg at intervals of not less than two days. The maximum dose is 3.0 g per day.

Examples of b.i.d. or t.i.d. dosage convenience provided by ALDOMET 500 mg within the usual daily dosage range of 500 mg to 2.0 g:

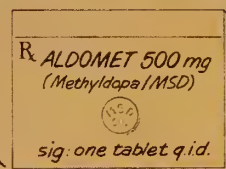
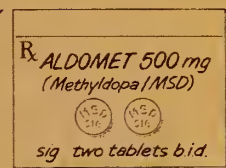
1.0-g
daily
dose =



1.5-g
daily
dose =



2.0-g
daily
dose =



NOTE: Tablets shown are not actual size.

in sustained moderate hypertension

ALDOMET[®] (METHYLDOPA|MSD)

usually lowers blood pressure effectively



Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis. Known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between six and twelve months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at six and twelve months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect

Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first six to twelve weeks of therapy or whenever an unexplained fever occurs. If fever, abnormalities in liver function tests, or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur.

Use in Pregnancy and Childbearing Age—Not recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Methyldopa may interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Stop drug if involuntary choreoathetoid movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has occurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure are occasionally seen and include dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency. Angina pectoris may be aggravated. Symptoms of orthostatic hypotension may occur; if symptoms occur, reduction of dosage is suggested. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distention, constipation, flatus, and diarrhea occur occasionally; these generally can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently and are relieved by administering a thiazide diuretic; if edema progresses or signs of pulmonary congestion appear, discontinue drug. A rise in BUN has been observed. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, Bell's palsy, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Note: Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Maximal recommended daily dose is 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

How Supplied: Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

MSD MERCK SHARP & DOHME

FIXED COMBINATIONS OF ANTIHYPERTENSIVE AGENTS

Diuretics and Rauwolfia Alkaloids

Diupres	Renese-R
Serpasil-Esidrix	Regroton
Hydropres	Rauzide
Exna-R	Hydroserp
Naquival	Reserpazide
Metatensin	Salutensin
Hydromox-R	Diutensen-R
Oreticyl	
Singoserp-Esidrix	

Diuretics and Potassium Chloride

Naturetin with K
Anhydron K

Diuretics, Rauwolfia, Alkaloids, and Potassium Chloride

Rautrax
Rautrax-N
Anhydron-KR

Diuretics and Sympathoplegic Drugs

Aldoclor (chlorothiazide and methyl dopa)
Aldoril (hydrochlorothiazide and methyl dopa)
Esimil (hydrochlorothiazide and guanethidine)
Combipres (chlorthalidone and clonidine)

Combinations containing Hydralazine

Serpasil-Apresoline (reserpine and hydralazine)
Dralserp (reserpine and hydralazine)
Apresoline-Esidrix (hydrochlorothiazide and hydralazine)
Ser-Ap-Es (hydrochlorothiazide, reserpine, and hydralazine)

Combinations containing Barbiturates

Butizide (hydrochlorothiazide and butabarbital)
Butiserpazide (hydrochlorothiazide, butabarbital, and reserpine)
Butiserpine (reserpine and butabarbital)
Sulfo-Serpine (reserpine, colloidal sulfur, and phenobarbital)

coincide with a patient's established needs. Combinations of hydrochlorothiazide and a potassium-sparing agent (i.e., Dyazide® or Aldactazide®) may occasionally be reasonable choices for initial diuretic therapy.

COMMENT

Essential hypertension is a serious disease, but its detection is easy and its treatment straightforward and effective. Unfortunately, antihypertensive therapy is not particularly gratifying to those involved. Patients resent the need for long-term treatment of an asymptomatic disease. Physicians may consider the disease uninteresting and often receive from their patients not gratitude, but complaints that the drugs are expensive and produce side effects. The problem of maintaining patients on faithful long-term therapy requires education of these patients and a visible commitment by the physician to long-term control of blood pressure. With a moderate effort, however, we can prevent the serious consequences of hypertension, a disease which is now described as a leading killer in our country.

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1974 IN REVIEW

Maine Blue Cross and Blue Shield met with many challenges in 1974, not the least of which was the economic crunch everyone found themselves in. Despite the economy, enrollment in the Plan increased, and a number of changes were made in benefits to meet the needs of subscribers and providers.

Claims Increase

Nearly 65,000 more Maine Blue Cross and Blue Shield claims were processed in 1974 than in 1973, and in its role as intermediary, over 36,000 more CHAMPUS and Medicare Part A claims were processed intermediately than in 1973.

In all, a total of 22,532 hospital claims and 449,347 were paid for group, non-group, Companion Plan, and Federal Employee subscribers, or 669,879 claims for both lines of business together. As intermediary for CHAMPUS and Medicare Part A, as well as administrator for the Blue Alliance Mutual Insurance Company, Maine Blue Cross and Blue Shield claims people processed an additional 238,950 claims.

Membership in all Maine Blue Cross and Blue Shield programs continued to increase in 1974, despite the recession. Group employee membership increased by 12,065 members to a total of 300,630, while non-group membership increased 1,042 to 143,442. Enrollment in the Federal Employee Program in Maine increased by 2,444 members to a total of 31,086. Total Maine Blue Cross and Blue Shield membership by the end of 1974 had reached a record of 475,158 Maine people.

Nineteen hundred and seventy-four was the second full year of operation for Coordinated Home Health Care program, and results show that out of the 170 patients admitted to the program, 1,733 patient days in the hospital were saved with a total estimated net dollar savings of \$74,681. With their doctors' permission, eligible patients living in the five Maine counties where the program is offered are allowed to go home to recuperate. Once home, the patients continue to receive skilled care in a relaxed familiar atmosphere.

The Coordination of Benefits (COB) program, initiated three years ago to help modify group coverage costs, has also proven to be quite successful. Savings of \$668,974.36 were accrued under this provision in 1974, and \$1,292,667.04 has been saved since COB was first introduced in 1972.

Coordination of Benefits means that Maine Blue Cross and Blue Shield agrees to share with commercial insurance companies all covered healthcare expenses when a subscriber is enrolled under more than one group healthcare program.

In this way, Maine Blue Cross and Blue Shield and the insurance companies eliminate the expensive duplication of payments that would exceed the actual cost of services the subscriber receives.

In general, the impetus of 1974 on strong cost efficiency features will be carried through into all new programs designed to meet the changing needs of our membership.

DYAZIDE[®]

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Each capsule contains 50 mg. of Dyrenium[®] (brand of triamterene) and 25 mg. of hydrochlorothiazide.

makes sense in edema.*

Neither inconvenient, unpalatable, expensive potassium supplements nor special K⁺ rich diets are needed as a rule. Just 'Dyazide' once or twice daily for control of edema.

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

*** Indications:** Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a

thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in

cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

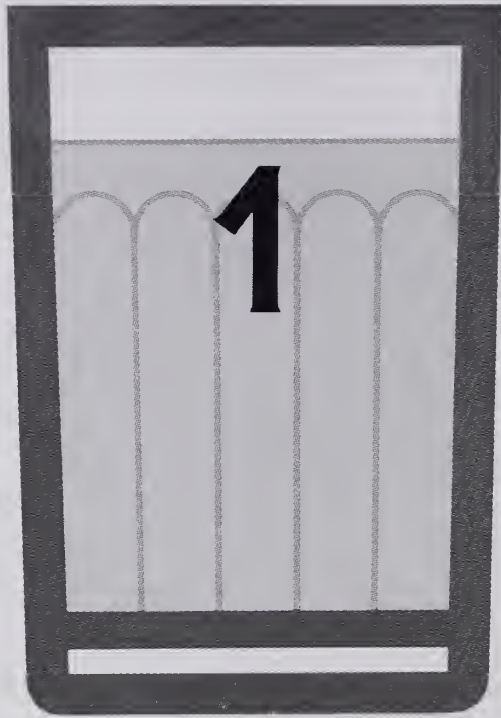
Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic non-obstructed urinary tract infections (primarily pyelonephritis, pyelitis, and cystitis) due to susceptible organisms. **Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials, including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprotrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, peri-orbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

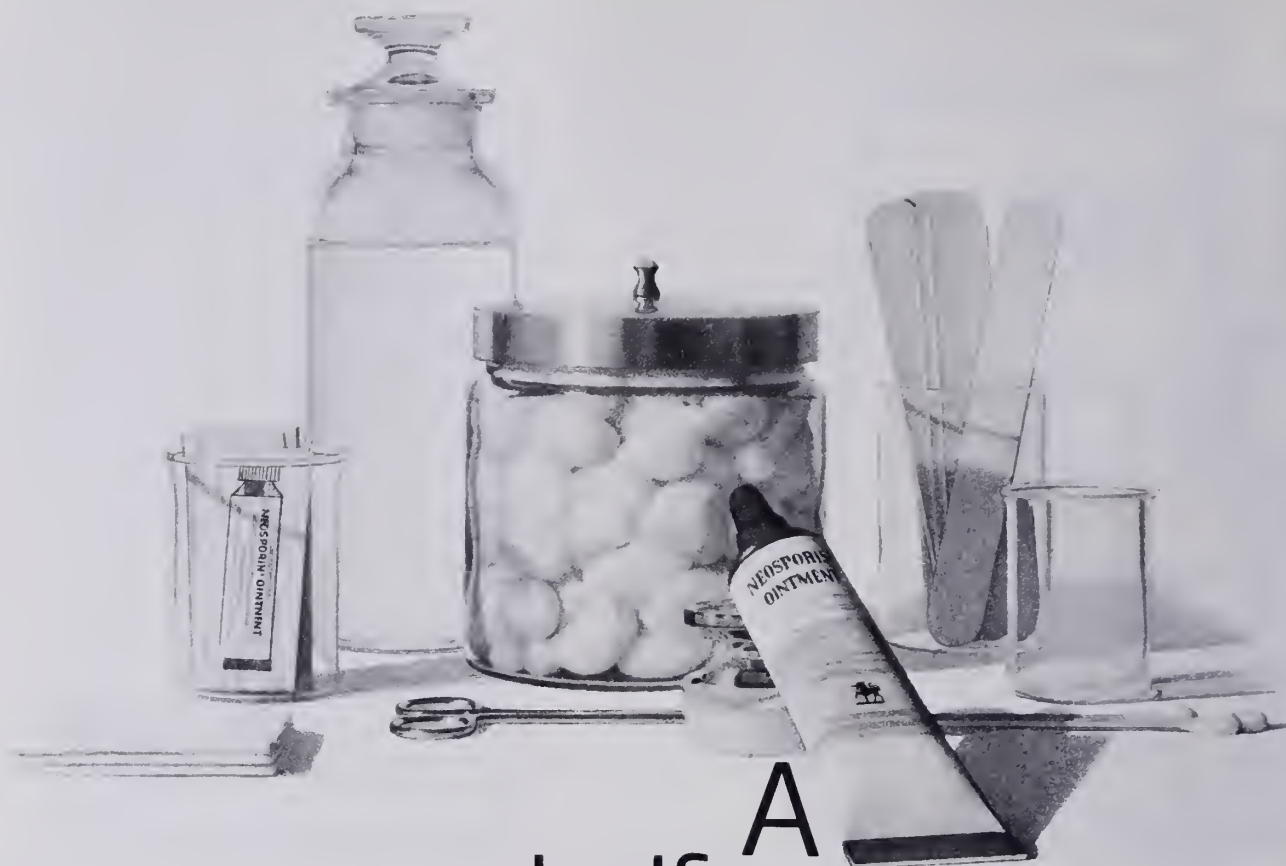
Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.



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In tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically*, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where

absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



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Editorial

A Tool For All Committees

Raw data is an unworthy substrate for final decision-making. Like crude oil, it has the necessary ingredients, but when used directly — it will only clog the gears of an operating process.

Health Care Delivery in Maine I: Patterns of Use of Common Surgical Procedures by J. E. Wennberg, M.D. and Alan Gittelsohn, Ph.D., published elsewhere in this issue, provides some raw and some partially refined data on common surgical procedures, and compares the frequency with which these procedures are performed in Maine and in Vermont.

This is an exciting and important work because it provides some answers to what, when, where and how often, and because it points the direction in which we must turn — to find the answer to, "why"! The "why"? is judgmental and good judgment will require thorough study and evaluation of the facts.

The weakest part of the article is the Dollar Projections. Starting with an unrealistic base — it moves into the never never land of speculation and ends up with unrealistic amounts to be conserved. But *don't* let that obscure the need to understand the hard factual data which is presented — and the very great need to answer as objectively as possible the question raised.

Why the variation in surgical procedure rates? —

Hemorrhoidectomies —

"Maine's highest rate exceeds Vermont's by almost 90%"

Hysterectomies —

"Are performed 40% more frequently in Maine than in Vermont"

Varicose Veins —

"Vermont outstrips Maine in its highest area by 80%"

Tonsillectomies —

"37% more in Maine than in Vermont"

All this will require a series of detailed looks by those who know the situation best — the Physicians themselves — this means time and effort, but the rewards are great; — a better understanding of the decision-making process in Medicine (Surgery), another parameter in the evaluation of patient care, and a chance to build a medical education program that is tailored to demonstrated needs.

The publication of this data will raise some hackles, but it will also give thoughtful Doctors cause to look at a new dimension, and to begin to talk about how to measure objectively the improvement of medical care.

DFH

HEALTH CARE DELIVERY IN MAINE I: PATTERNS OF USE OF COMMON SURGICAL PROCEDURES

Continued from Page 130

gest they occur because of differences in opinion among physicians concerning the effectiveness of specific treatments or in the way physicians define health care needs. Differences in opinion may in some cases relate to differences in the rate of diffusion of new knowledge about medical practices. Agreement may be fostered or differences resolved by participation of two or more physicians in decision making at the individual case level. However, in some cases, professional uncertainty may be resolved only by empirical studies on outcome. A role in the undertaking of activities to deal with geographic variations is suggested for quality assurance programs.

ACKNOWLEDGMENTS

This analysis has been made possible through the cooperation and support of many individuals, associations and agencies. The principle parties who provided funds are the Maine State Comprehensive Health Planning Agency and Maine's Regional Medical Program. Responsibility for data collection and tabulation were jointly shared by Maine's Data Service and the Cooperative Health Information Center of Vermont. The effort has been made possible by the willingness of the individual hospitals in Maine to participate in a State-wide data system.

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County Society Notes

CUMBERLAND

The 392nd meeting of the Cumberland County Medical Society was held on January 17, 1975 at the Union Mutual Building. One hundred and ninety-nine members and wives attended. The social hour was a pleasant interlude, followed by a well-prepared buffet dinner.

A brief business meeting was called to order by the President, Dr. Stanley B. Sylvester at 8:30 p.m. Dr. Noel C. Goodman was accepted into membership as a transfer from Androscoggin County. Dr. Anthony F. Salvo was transferred from junior to active membership.

Donald R. Larrabee, the well-known newspaper and television correspondent, was then introduced by Dr. Sylvester. Mr. Larrabee gave an interesting and informative presentation concerning Congress at the Crossroads. A lively discussion followed his talk.

The meeting was adjourned at 10:15 p.m. by Dr. Sylvester.

ALFRED E. SWETT, M.D., *Secretary*

KENNEBEC

A meeting of the Kennebec County Medical Association was held at the Holiday Inn in Augusta, Maine on February 20, 1975. Following a cocktail hour and dinner, the President, Dr. Joseph J. Hiebel called the meeting to order.

Minutes of the January and December meetings were dispensed with.

The applications of Drs. Albert Pepe and Helen Mitchell were

read. The Association accepted into membership Dr. Joseph R. Metz. The transfer of membership of Dr. Henry C. Thacher from the Androscoggin County Medical Society was noted.

Correspondence: Dr. O. Thomas Feagin reported that Dr. Daniel Hanley of the Maine Medical Association had called requesting members to make themselves available for appearing in Legislative hearings on Tuesday, February 25th, in regard to several bills and that he had requested members to write the Legislative Committee on Labor. A vehement discussion about the Legislature ensued. Some of the members said that they would like to be better informed of the proceedings relative to medicine in the Legislature. It was decided to hold a special Council meeting before the next regularly scheduled meeting to discuss this matter and such a meeting will be called. Dr. Hiebel suggested that perhaps a Committee to deal with legislative matters on the county level should be appointed to work with the State Legislative Committee. Dr. Peter J. Leadley of the Maine Department of Health and Welfare and Joseph Hasenfus of RMP presented to the Council material relating to the Tel Med program. This material was presented to the full meeting and a vote was taken. The Association voted to endorse the concept and not at the present time to commit any funds pending the decision of the State Society.

Scientific Session was then held under Dr. Albert Dibbins of the Maine Medical Center, presenting a most enlightening talk on the subject of intestinal obstruction in the newborn.

The meeting was adjourned at approximately 10:15 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

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Volume Sixty-six

Brunswick, Maine, June 1975

Number 6

Ureteral Calculus in Pregnancy and the Puerperium

JOHN ZERNER, M.D., F.A.C.O.G.*

Over the past years, several cases of ureteral calculi occurring in pregnant patients have been observed. Because of the rarity of occurrence, as well as the wish to stimulate general medical interest, these representative histories are presented and discussed.

CASE 1

T.M.T., a 29-year-old, Gravida III, Para II, 18 weeks gestation was admitted to the Mercy Hospital on 5/19/69 with left CVA pain of four hours duration. Antepartum course to that date had been essentially within normal limits.

Lab studies: CBC: Hematocrit 41, WBC 13,700 with shift to the left. Urinalysis: 15-25 RBC/hpf, 2-4 WBC/hpf. Urine culture showed *E. Coli* sensitive to Ampicillin. An Antibiotic (Ampicillin) was initiated and the patient was discharged without symptoms, the next day.

She was readmitted on 5/25/69 with exacerbation of left CVA pain along with nausea and vomiting. An IVP was obtained (2 views); a left intramural ureteral stone with partial obstruction of the left ureter, was demonstrated. The calculus passed spontaneously. It was described as weighing 30 mg., being light tan in color, hard, non-crystalline and composed of calcium carbonate.

Following discharge, antibiotics were continued. Pregnancy progressed and she delivered uneventfully at term.

CASE 2

R.E.S., a 23-year-old, Gravida II, Para I, with EDC 10/21/73, admitted at 29-weeks gestation to the Mercy Hospital on 7/10/73, with "shooting" right lower-quadrant pain extending into the internal portion of her right thigh. Past History: A left renal stone was noted three years prior to the present pregnancy.

Lab studies: CBC: Hemoglobin 10.3, with WBC showing a shift to the left. SMA 12/60: within normal limits. Urinalysis: 100 WBC/hpf.

Patient was observed and then discharged after 24 hours, being placed on Erythromycin 250 mg. p.o., q.i.d. She was readmitted 7/15/73 with exacerbation of symptoms. Keflin® was then initiated, during which time she was asymptomatic. The patient was observed for three days in the hospital and then discharged.

*Mercy Hospital Medical Staff, 144 State Street, Portland, Maine 04101.

On 7/27/73, the patient spontaneously passed a brownish calculus composed of magnesium phosphate and ammoniate.

The patient delivered 10/26/73 a male infant via cesarean section for CPD.

CASE 3

R.L., a 22-year-old patient, Gravida I, Para I, delivered a full-term infant on 4/14/71. During pregnancy, at 26 weeks gestation, she developed left CVA pain, chills, fever, and a mass of the left flank. Antibiotics were initiated on the presumptive diagnosis of left hydronephrosis and pyelonephrosis and pyelonephritis. An IVP obtained following delivery, demonstrated one stone in the left ureter at the junction of the upper two-thirds and the lower one-third of the ureter, as well as two stones in the collecting system on the left.

Lab studies: SMA 12/60 all within normal limits. Creatinine clearance: 56 cc. per minute. Urine culture and sensitivity revealed enterobacter, sensitive to Keflin.

On 4/19/71, cystoscopic examination, bilateral ureterography and left ureterolithotomy were performed, with the removal of a stone measuring 2.7 cm. x 0.8 cm. x 0.6 cm. The stone was yellow and composed of calcium, phosphate, magnesium carbonate and ammonium carbonate. Uric acid and cystine were not present. Patient did well following surgery and was discharged 4/26/71.

She was readmitted 5/7/72 and at this time cystoscopic examination, IVP, and bilateral retrograde studies were all considered normal. Urine cultures of bladder and both kidneys showed no growth.

CASE 4

D.T., a 25-year-old Gravida I, Para 0, EDC 12/7/74, was admitted to the Maine Medical Center on 10/1/74 at 30 weeks gestation complaining of right CVA pain of six hours duration, compatible with acute right pyelonephritis. To that date, her ante partum course had been without abnormality. Prior medical and surgical history was unremarkable and no history of previous urinary tract infection or calculus could be obtained.

Lab studies: SMA 12/60: within normal limits. CBC: Hematocrit 34.7, WBC 13,900 with a shift to the left. Urinalysis: S/G 1.016, > 100 RBC/hpf, 35-40 WBC/hpf. Urine culture and sensitivity was obtained on admission, prior to antibiotic therapy, and showed no growth.

Ampicillin was initiated intravenously. As the pain continued unabated, a modified IVP (20 minute and 2 hour films) was

obtained showing markedly delayed function of the right collecting system; in essence, only a right nephrogram was seen at two hours.

Additionally, a radiopaque density was seen in the distal one-third of the right ureter with ureteral dilation proximally. Approximately 12 hours later a single calculus was passed. The calculus weighed 45.2 mg., and was composed of an irregularly laminated mass of subcrystalline hydroxyl apatite.

Spontaneous labor ensued on 11/25/74, with vaginal delivery of a male infant weighing 7 lbs., 15 ozs. Her post partum course was uneventful. Repeat SMA 12/60, urinalysis, urine culture and sensitivity were reported as showing no abnormality.

CASE 5

C.N., a 29-year-old Gravida IV, Para III, with EDC 3/17/74, was admitted to the Maine Medical Center on 2/5/71 with severe right CVA pain. IVP studies showed an apparent 0.5 cm. calculus in the right lumbar ureter. Conservative therapy was initiated; her pain disappeared and she was discharged five days later. On 3/4/71, repeat cesarean section was performed uneventfully.

The patient was readmitted on 8/16/71 with acute abdominal pain. The diagnosis of cholecystitis was entertained, but was not proven. On the basis of the previous ureteral calculus, a repeat IVP was obtained, showing a normal left system, but with longstanding right pyelonephritis, as evidenced by contraction and scarring. There was again an apparent right ureteral stone at the ureterovesical junction.

In 1972, further radiographic studies were performed, obtaining oblique views of the right lumbar region. It then became possible to demonstrate the calcification noted previously was not a right ureteral stone, but rather an osteochondroma of the right sixth rib.

Ureterolithiasis is an unusual occurrence in pregnancy.⁸ Hellman⁴ quotes an incidence of 0.08 percent in approximately 10,000 deliveries. Semmens,⁹ on the other hand, has reported 9 cases occurring as a complication during 2037 full term deliveries, an incidence of 1:286.

There seems to be a fairly even distribution of cases throughout each trimester and into the puerperium.² The age of patients does not follow any strict pattern. Parity, however, seems to be important. In our cases, two of four were primigravids and this finding is apparently confirmed by others^{2,5,9,3} who have recorded the greater number of ureteral calculi occurring during the first pregnancy.

Symptomatology may vary, secondary to the site of obstruction. If the calculus is located at the pelvic brim or below, ureteral colic is noted; if above the brim, renal colic is the more common.⁵ Painful hematuria is rare.³

Three areas are involved where calculi may cause obstruction: 1) The region of the mid one-third ureter where the infundibulopelvic vessels cross over the underlying ureter 2) The pelvic brim, and 3) The ureterovesical junction. In addition, the upper two-thirds of the ureter will undergo dilation secondary to mechanical and hormonal changes occurring during pregnancy, while the distal one-third, the "pelvic ureter," does not.⁵

The location of the calculus seems to be a function of its size. Those of 1.1 cm. or less in diameter are found either in the pelvic ureter or at the ureteroves-

ical junction. Calculi of 1.5 cm. or more, however, are most commonly noted in the upper ureter.⁵ Harris³ and Semmens⁹ state there is no special predilection for either the right or left side while Folger² describes another series with the right ureter being involved twice as commonly as the left.

Pregnancy outcome has been, in general, successful. Of 19 cases described by Harris,³ all were delivered of viable term infants. On the other hand, Folger² describes several patients requiring termination of pregnancy. However, it is to be emphasized that all had renal disease of many years standing and that termination was done only in the face of far advanced, irreversible, and progressive renal disease, or in the presence of a dead fetus. Further, all cases occurred prior to 1955.

Adequate evaluation of the urinary tract is to be emphasized.¹² Blood levels of phosphorus, calcium, and alkaline phosphate are done in an attempt to rule out possible parathyroid gland tumors.⁴ Low levels of phosphorus are more indicative of these parathyroid tumors than high calcium levels. The composition of the calculi is important to rule out the presence of xanthine, uric acid or cystine, which occur in acidic urine and might be benefited by an alkaline diet. Culture and sensitivity of the urine must be obtained to rule out any underlying urinary tract infections.

Radiologic studies should be utilized but the benefits derived from the examination must always be balanced against the unknown risks of radiation.¹ However, pregnancy is not to be considered a contraindication to the judicious use of x-ray. It is to be remembered that geneticists advise the average individual's exposure to radiation not exceed 10 R. from conception to age 30.⁶ Natural radiation contributes 3 R. in total during this 30-year span and nuclear fallout will contribute an estimated 0.01 R. per year. An intravenous pyelogram of 4 to 6 views would expose the gonads of mother and fetus to between 0.4 R and 1.6 R., depending on the methods employed. Therefore, to lower radiation exposure, a suggestion is made to obtain a "modified IVP" consisting of two views: a preliminary film and then following dye injection, a 20 minutes view. Of course, further studies would be obtained if necessary.¹¹

Treatment must be individualized in every patient.^{2,3,9} The concept of a *coordinated team*⁹ — obstetrician and urologist, must be emphasized and used to evaluate each case. Early recognition of the possibility of ureteral calculi significantly aids in the prognosis,^{1,8} allowing for vigorous diagnostic and therapeutic measures to be instituted. Delays in diagnosis and definitive treatment may well result in permanent renal damage and could jeopardize the outcome of the pregnancy.⁹ Several factors contribute to therapy: 1) The date of pregnancy, 2) Loca-

tion of stone, 3) Presence or absence of obstruction and infection, 4) renal function, and 5) The general condition of the patient.⁸

Generally, conservative therapy (i.e., hydration, correction of any electrolyte imbalance, straining of all urine, and the appropriate use of antibiotics after culture, sensitivity and colony count have been obtained) will suffice as in over fifty percent there will be spontaneous passage of the calculus.³ Yet, for those in whom there is no clinical improvement, surgery may be indicated.

The procedure of choice is dependent upon the current stage of pregnancy. In the first trimester, active intervention is indicated if symptomatology or signs of obstruction increase. Direct surgery upon the ureter, either via endoscopic manipulation or transabdominally, is permissible. Neither the uterine size nor pelvic vascularization will interfere. The same may be said for surgery in the second trimester. However, in the last trimester (after 27-28 weeks gestation) direct exploration of the pelvic ureter attempted endoscopic manipulation of the ureteral calculus is contraindicated; first, because of the increased pelvic vascularization and secondly, due to the enlarging uterus which obscures direct visualization of the involved area. Nephrostomy is often the procedure of choice to alleviate obstruction and attempt to salvage renal parenchymal tissue.³

Most importantly, termination of pregnancy for unilateral urinary tract obstruction, secondary to ureterolithiasis, is not indicated.

The case of any patients with suspected or proven calculi must continue beyond the delivery and puerperium.⁷ Persistence by the physician in obtaining meticulous follow-up is to be encouraged. Blood and urine analysis, repeat IVP or other radiographic studies, where necessary, are indicated should there be any doubt in the diagnosis. Indeed, case #5 demonstrates the time and effort involved to arrive

at a correct (and unexpected) wholly new diagnosis.

In summary then, a series of cases were presented by ureteral calculi occurring during pregnancy. The general characteristic of these patients' symptomatology and treatment are discussed. Emphasis is placed on a coordinated team approach with appropriate evaluation both in the ante and postpartum periods.

ACKNOWLEDGMENT

My deepest thanks to Mrs. Diane Kneeland, Drs. Alfred E. Swett, Andrew P. Iverson, and Robert P. Timothy for their assistance and encouragement in the writing of this paper.

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Reminder to M.M.A. Members

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Blood Cultures in a Community Hospital

JOHN D. RICE, JR., M.D.* and JUNE L. ATHERTON**

Bacteremia is detectable by culturing blood in suitable nutrient media. The procedures for processing blood cultures in the microbiology laboratory are relatively uncomplicated, but it is quite another matter when it comes to the problem of how many blood cultures should be obtained in a given clinical situation, and the frequency with which these blood cultures should be obtained. Physicians vary greatly in their approach to the clinical situation of a patient with possible bacteremia. Some will order one or two cultures, others favor multiple cultures drawn at stipulated intervals of time, or timed in relation to some observed event such as a chill. The laboratory faces situations in which it processes one or two blood cultures from one patient, and perhaps a dozen cultures from another patient. Since each blood culture bottle received in the microbiology laboratory must be subcultured to definitive media, the processing of a large series of culture bottles from a single patient can fully occupy the workday of a microbiologist in the laboratory. The problem of patient care also arises. It is well known that the likelihood of obtaining a positive blood culture after instituting antimicrobial therapy is very small. The concerned physician faces the problem of obtaining sufficient blood cultures to insure recovery of organisms when present, yet not delaying institution of antimicrobial therapy, and increasing the risk to his patient. In order to ascertain whether past experience at Mercy Hospital could add to solutions for these problems, an internal study was made of all blood cultures submitted to the microbiology laboratory in the period 1970-1973. The results of that study are presented in this report.

MATERIALS AND METHODS

During this period, blood cultures were made by laboratory phlebotomists on orders from staff physicians. Cultures were usually drawn from an arm vein after routine preparation with iodine and alcohol. In the early part of the period of study routine cultures were taken with a sterile syringe, or by directly introducing 5 ml of blood through a sterile double needle and plastic tube set from the vein to a 50 ml bottle of thioglycollate broth with added carbon dioxide atmosphere. Later in the study, and in current use, the volumes were

changed to 10 ml of blood in 100 ml of thioglycollate broth with added carbon dioxide. Present laboratory protocol calls for the substitution of trypticase soy broth in a carbon dioxide atmosphere for thioglycollate broth. Also 0.025 percent sodium polyanethol sulfonate (SPS) has been added to all bottles as an anticoagulant and antileukocyte agent.

Bottles were stored at 37°C without venting, and were examined daily for evidence of growth.

After overnight incubation, the bottles were entered with a sterile syringe. Gram stains were prepared, and subcultures were made to blood agar and chocolate agar. The blood agar plate was incubated anaerobically, and the chocolate agar plate was incubated in a 6 percent carbon dioxide atmosphere. If the Gram stain disclosed organisms, further appropriate subcultures were prepared. If no growth occurred in the blood culture bottle or subculture plates, a second subculture from the original bottle was made on the 10th day. These final subcultures were incubated for 48 hours before discarding material as showing no growth.

RESULTS

In the period 1970-1973, there were 1,896 blood cultures drawn. Of these, there were 136 which showed bacterial growth, an incidence of 7.2 percent. Of the patients with positive cultures, 92 percent showed growth in one or both of the first two cultures drawn without regard for the frequency with which cultures were drawn. Table 1 shows results on a yearly basis.

Table 2 shows the variety of organisms recovered from patients with positive blood cultures. In certain instances the nature of the organism, and the pattern of growth suggest that the organism was a contaminant.

DISCUSSION

Published material on the subject of blood culture generally makes a distinction between blood cultures in cases of subacute bacterial endocarditis, and blood cultures in non-endocarditic bacteremia.^{1,2} Also, there are a small number of special conditions such as suspected brucellosis in which the nature of the organism demands special techniques for culture, and isolation. The latter are not considered here.

In patients with documented bacterial endocarditis, the magnitude of bacteremia is relatively constant.³ The number of bacteria in a milliliter of blood in endocarditis may be as small as 1-30. In

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TABLE 1
BLOOD CULTURES AT MERCY HOSPITAL, 1970-1973

	1970	1971	1972	1973
Total Blood Cultures	298	490	496	612
Total Patients Involved	131	229	216	208
Average Cultures per Patient	2.3	2.1	2.3	2.9
Total Positive Patients	17	17	16	22
Percent Positive Patients	13.0	7.4	7.4	10.6
Total Positive Cultures	27	31	32	46
Percent Positive Cultures	9.1	6.3	6.4	7.5
Patients first positive in first culture	82%	76%	88%	82%
Patients first positive in second culture	6	18	12	14
Patients first positive in third culture	12	6	—	—
Patients first positive in fourth (or greater) culture	—	—	—	4*

*Six blood cultures drawn rapidly within a few minutes of each other. All were sterile except for diphtheroids recovered from the sixth culture.

TABLE 2
ORGANISMS RECOVERED IN POSITIVE BLOOD CULTURES

Organism	Number of Patients			
	1970	1971	1972	1973
<i>Gram Positive</i>				
Coagulase pos. staphylococci	2	4	1	3
Coagulase neg. staphylococci	1		3	3
Alpha hemolytic streptococci	2	4	2	2
Strep. pneumoniae	2		1	3
Clostridium perfringens		1		
Beta hemolytic, group A streptococci		1		
Anaerobic streptococci			1	
Bacillus subtilis			1	
Diphtheroids			1	2
<i>Gram negative</i>				
E. coli	6	2	2	2
Bacteroides fragilis	2	2	3	2
Proteus mirabilis	1			2
Proteus rettgeri		1		
Providencia spp.	1			
Hemophilus spp.		1		
Serratia marcescens		1		
Enterobacter cloacae			1	1
Klebsiella pneumoniae				1
Neisseria meningitidis				1

non-endocarditic bacteremia there is often associated chills, fever, and/or shock. This implies relatively greater numbers of organisms present per milliliter of blood, and, possibly, the presence of bacterial toxins. Most published information indicate that one, or, at most, a few cultures will serve to isolate organisms in non-endocarditic bacteremia.^{4,5,6} An extensive study of 206 cases of bacterial endocarditis made at New York Hospital-Cornell Medical Center over the period 1944-1960³ indicates that, where streptococci were involved, the first blood culture was positive in 96 percent of cases. In non-streptococcal endocarditis, the first blood culture was positive in 82 percent of cases, and one of the first two cultures was positive in all cases. Petersdorf⁵ recommends 1-2 cultures be obtained in febrile patients with suspected non-endocarditic bacteremia. Cultures obtained after instituting antimicrobial therapy are worthless. In

suspected bacterial endocarditis, he obtains 6 blood cultures at the rate of 2 per day for 3 days. On the other hand, if there is good clinical evidence of endocarditis, he is satisfied with 2-3 cultures obtained over a short period of time before therapy is instituted.

The data obtained in the Mercy Hospital study support current opinion that large series of blood cultures do not improve the likelihood of isolating a causative organism either in cases of bacterial endocarditis or in non-endocarditic bacteremia. Also, a prolonged series of blood cultures complicates laboratory processing, and invites errors leading to the growth of contaminants. There is also a tendency for physicians to delay institution of therapy while hoping for a few of a long series of cultures to show growth. This may work to the detriment of the patient.

Continued on Page 157

Puerperal Intestinal Obstruction

A Presentation and Discussion

JOHN ZERNER, M.D., F.A.C.O.G.* and WALTER B. GOLDFARB, M.D., F.A.C.S.

Reports of intestinal obstruction occurring during pregnancy are not frequently seen in the literature.² Obstetrical textbooks have given but a brief mention of this problem.⁷ Further, intestinal obstruction during the puerperium is extremely rare³ and it is for this reason that the following case is presented.

CASE REPORT

A 34-year-old female, G₂P₁, EDC 7/25/74, was admitted to the Maine Medical Center in active labor on 7/7/74. Her antepartum course was essentially benign. Laboratory studies: Rh positive. Rubella titer 1:32. CMV titer 1:16. Toxoplasmosis 1:32. Urine: Negative. SMA 12/60: Within normal limits. Urine C&S: No growth. Hct: Stable, ranging 36-37.

One previous pregnancy (1973) was uneventful with delivery of a female infant weighing 6 lbs. 6 ozs., under saddle anesthesia after a 9-hour labor.

Her past history is significant in that she underwent right oophorectomy and incidental appendectomy in 1951. Spinal fusion was performed in 1963. During 1969-73, the patient had multiple urinary tract infections treated medically; an IVP in 1970, moreover, was essentially within normal limits.

Patient's course in labor was marked by greater than usual pain during and continuing beyond each contraction to such a degree that the attending physician entertained the diagnosis of partial abruption; appropriate studies, however, were considered within normal limits. Spontaneous vaginal delivery of a 7 lbs. 3 ozs. male infant occurred after 2 hours and 44 minutes of labor with a midline episiotomy and saddle anesthesia. The second stage of labor is best described as precipitous, lasting only 4 minutes. Exploration of the endometrial cavity was unremarkable and estimated blood loss was 250 cc. The placenta gave evidence of marginal separation with a succenturiate lobe. During the immediate post-partum, the patient complained of intense crampy right-sided abdominal pain. The possibility of retained products of conception was considered and she underwent EUA and D&C during which a moderate amount of blood clots and decidual tissue was obtained.

Following this surgery, pain, while present, decreased somewhat and remained to the right of the midline; the patient was kept NPO and continual IVs were administered. On 7/9/74, a Levine tube was inserted after pain seemed to be localizing in the right upper quadrant. The possibility of acute cholecystitis was entertained. Abdominal films showed distension in the proximal jejunum consistent with partial small bowel obstruction. On July 10th, she continued afebrile; the abdomen was flatter and softer with RUQ tenderness still present. Over the next 48 hours, however, abdominal distension increased gradually along with a concomitant decrease in bowel sounds. Dull pain became suffused throughout the abdomen and repeat x-rays showed partial obstruction in the mid- or distal jejunum; the impression was obstruction secondary to adhesions from previous abdominal surgery.

Exploratory laparotomy was performed on 7/12/74. An adhesive band went across the mid-ileum, producing a narrow steno-

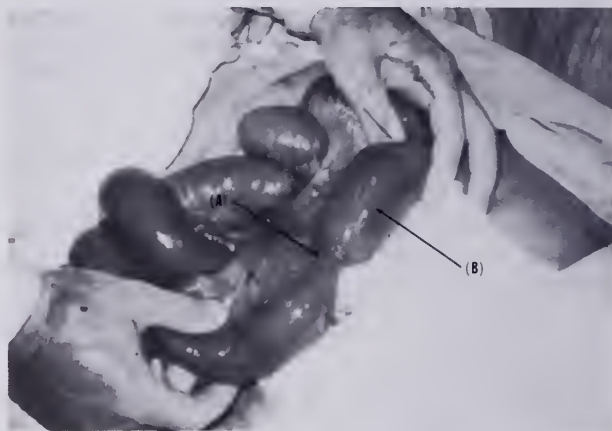


Fig. 1. Photo demonstrating (a) Stenotic segment of bowel-later resected- and (b) dilated segment of ileum proximal to the obstruction.

tic segment of bowel with a dilated three-foot segment of ileum proximal to the adhesion (Fig. 1). The band was lysed and excised. The stenotic segment of bowel, as it appeared compromised, was resected and a primary anastomosis performed. Postoperatively, the patient did well and was discharged on 7/22/74.

DISCUSSION

The pregnant woman with an abdominal scar must always be considered a candidate for intestinal obstruction. Occurring in pregnancy, obstruction can be a fatal condition.^{3,4,6} The small intestine is involved most frequently and any form of obstruction to that portion of the bowel leads invariably to early gangrene and the necessity of resection. Incidence of this complication during pregnancy itself is very low and is extremely rare during the immediate post-partum period. Waters,⁶ in a survey of 115,000 deliveries at the Margaret Hague Maternity Hospital, reported only 6 cases and, of these, only one occurred following delivery. Weintraub⁷ described 4 cases in a series of 32,000 deliveries with but one in the puerperium. In more than 75% of the total cases studied, obstruction was found to be involved with adhesions secondary to previous abdominal surgery.

The acute episode during the early post-partum, arising from adhesions already present, may be explained by the changes occurring after the sudden decompression of the uterus and abdomen. There is extensive re-arrangement of the intestines, often with a sudden rush of gas into bowel proximal to an

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adhesion. The resultant distension of this bowel followed by torsion would then lead to the picture of intestinal obstruction.

Diagnosis is difficult and often delayed⁷ as usual parameters are unreliable.^{1,5} First, symptomatology can be minimal or, as in the case presented, be seen to mimic other entirely unrelated problems. Secondly, the enlarged uterus fills the pelvis and lower abdomen, blocking to examination the two most common sites — pelvic and right iliac region — where 7 of 10 strictures occur secondary to post-operative adhesions and bands. X-ray studies are often distorted by the gravid uterus; in addition, post-partum hypotonicity of the bowel may mask obstruction. It is to be emphasized, however, that *repeated* x-ray studies of the abdomen are valuable to demonstrate *progressive* changes that may be suggestive of intestinal obstruction: Continued distension of bowel loops, air-fluid levels, and so on. Neither CBC nor electrolyte studies are as accurate; the former as the cell count is elevated and shifted slightly to the left during the late stage of pregnancy; the latter due to the rapid changes in body fluids from one compartment to the other occurring in the puerperium.

A high index of suspicion is the indispensable prerequisite to timely diagnosis and rational treatment.^{1,4} Ancillary methods, i.e., intubation, the use of intravenous fluids for replacement therapy and electrolyte balance, systemic antibiotics — are to be used only to prepare for, and not to take the place of surgery.^{2,4}

Therapy, once the diagnosis of obstruction is made, becomes clear-cut: Immediate exploration and the performance of a procedure appropriate for

the individual situation. Surgery must not be delayed even in the presence of pregnancy.³ Mortality increases the longer one procrastinates. Earlier accounts of "expectant observation" carry descriptions of a prolonged course leading inexorably to perforation, peritonitis, septic shock and eventual death.^{5,6}

In summary, a statement made thirty-five years ago, still holds true: "Pregnancy predicates pernicious procrastination in the management of obstructions".⁷ This is to be condemned. Aggressive management of the pregnant female with intestinal obstruction must be emphasized to insure survival of both the mother and the child.

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BLOOD CULTURES IN A COMMUNITY HOSPITAL — *Continued from Page 155*

The Mercy data were obtained under conditions in which a single culture was taken; several cultures were taken in rapid succession, or cultures were spaced over a period of days. Organism recovery records do not suggest that there is much to be gained by ritualistic adherence to any particular plan for timing of cultures. This has been noted in recent reviews.^{2,6} Especially where bacteremia is continuous, as in endocarditis, or relatively massive such as in fulminating infections, there is little difference whether blood cultures are taken over a brief period, or whether they are spaced over a longer time. If intermittent bacteremia is suspected, there may be some merit in spacing cultures to precede clinical manifestations such as chills or fever rise.

The fundamental consideration in all cases of possible bacteremia or septicemia is the urgency of the clinical situation. Certainly the institution of lifesaving antimicrobial therapy should not be de-

layed in the mistaken belief that many blood cultures are required to recover an organism. It would appear that, even if the blood density of organisms is very low, modern microbiological techniques are well geared to recover them in culture. The physician can be assured that a few properly obtained blood cultures are as effective as half a dozen or a dozen. Excessive numbers of blood cultures offer no advantage, and can result in harm to the patient.

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Adult-Onset Aqueductal Stenosis

WILLIAM H. LESCHEY, JR., M.D.* and TIBOR DOBY, M.D.**

Stenosis or narrowing of the Sylvian aqueduct can occur on a congenital, inflammatory, neoplastic, or traumatic basis. Aqueductal stenosis is a well known cause of hydrocephalus in childhood. Non-neoplastic aqueductal stenosis does occur in adults, and creates unique problems in diagnosis and management.

CASE REPORT

A 31-year-old construction worker was admitted to the Mercy Hospital on 7/8/74 for evaluation of dizziness, headache, and a solitary blackout spell. For about 8 months, the patient has had intermittent headaches, usually generalized, but sometimes more intense at the vertex. The headaches increased with coughing, sneezing, straining at stool, and with rapid head motion. He also complained of positional dizziness, and would at times experience severe vertigo with nausea after sudden changes in posture. These attacks would only last for minutes at a time, and he denied tinnitus and hearing loss. Four months prior to admission, he fell down unconscious during micturition. There was tongue biting, but no observed rhythmical jerking, bladder, or bowel incontinence. Friends had commented that he had undergone a personality change, and the wife confirmed this. He had no difficulty with memory. His walking was impaired only during the dizzy spells. There was no history of meningitis, encephalitis, or head injury.

On examination, he appeared as a robust, healthy looking, 180 lb., 5'-11" man with a head circumference of 58 centimeters. Fundi revealed some blurring of the nasal optic disc margins bilaterally, and absent venous pulsations. A few beats of horizontal jerk nystagmus occurred on positional testing. The pupillary and oculomotor responses were otherwise normal including optokinetic testing. No cerebellar signs were present. He walked well on the toes, heels, and in tandem. Deep tendon reflexes were symmetrical. Plantar responses were flexor bilaterally. No sensory findings were present.

Skull films, EEG including sleep, and brain scan with radioisotope flow study were all normal. Right retrograde brachial and left carotid angiograms indicated symmetrical enlargement of the lateral ventricles. In the lateral views, the pericallosal arteries showed stretching and an enlarged sweep (Fig. 1). In the anteroposterior views, the thalamostriate veins were bowed, and displaced laterally (Fig. 2).

Pneumography via the lumbar route showed an undisplaced, normal sized fourth ventricle (Fig. 3). The pericallosal cistern was elevated and arched. There was no air fill in the lateral or third ventricles. CSF protein was 35 mg. percent. A right frontal ventriculostomy was carried out. Opening pressure was 500 mm. and the cerebral mantle measured 2½ centimeters in depth. Air introduced from above showed marked symmetrical enlargement of the lateral and third ventricles, and dilatation of the rostral portion of the aqueduct (Figs. 4 and 5). Superimposition of lateral views of the pneumoencephalogram and ventriculogram indicated aqueductal occlusion (Figs. 3 and 5).

On August 21, 1974, the patient underwent ventriculo-atrial shunting with a medium sized Holter valve. His postoperative course was afebrile and uncomplicated. He had no more headaches, dizziness, or episodes of loss of unconsciousness. Five weeks after surgery, he returned to work. He continues to

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Fig. 1. Lateral view of right retrograde brachial angiogram shows stretching and an enlarged sweep of both pericallosal arteries.

do well, and remains asymptomatic. Friends have noted that now "he is his old self."

DISCUSSION

The pathology of non-neoplastic aqueductal stenosis has been well described by Russell.¹⁰ The classification includes simple stenosis, forking or atresia, septum formation, and gliosis. Simple stenosis, a histologically normal but narrow aqueduct, and forking or atresia of the aqueduct are considered congenital or developmental anomalies. Septum formation may be a congenital malformation, or the result of inflammation. The cause of periaqueductal gliosis is unsettled, and much debated. The limitations of the classification itself and the implications about etiology have been discussed.¹ A single case may show forking, gliosis, and inflammatory changes in serial sectioning of the aqueduct.¹



Fig. 2. Venous phase AP view of left carotid arteriogram reveals bowing and lateral displacement of the thalamostriate vein.



Fig. 4. Frontal projection of ventriculogram shows dilated lateral ventricles.

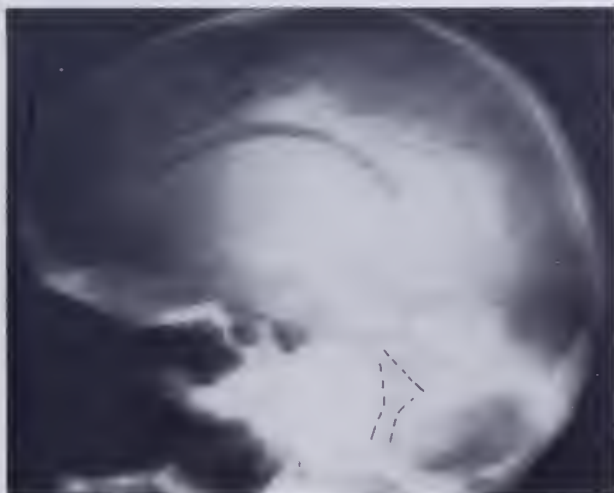


Fig. 3. Lateral view of pneumoencephalogram shows a normal fourth ventricle (dotted lines), elevated and stretched pericallosal cistern, but no filling of the lateral ventricles or third ventricle.



Fig. 5. Lateral view autotomogram of ventriculogram reveals dilated lateral and third ventricles. The dilated rostral portion of the aqueduct ends abruptly.

Regardless of the type of pathology causing aqueductal block, Russell postulated that dilatation of the pathways proceeded in a retrograde fashion to the lateral ventricles. The normal exit pathway of CSF produced in the lateral and third ventricles is obstructed at the aqueduct. Hydrocephalus with enlargement of the lateral and third ventricles is the consequence. This traditional concept has been recently challenged.¹⁴ Evidence that aqueductal stenosis may be the result of hydrocephalus, rather than the cause, has been presented. A CSF absorptive defect distal to the aqueduct is hypothesized as causing lateral ventricular dilatation. Subsequent downward displacement of the tentorium and hind-brain occur and in turn may cause compression of the mid-brain between the hemispheres. Mid-brain compression would compromise the aqueduct. This mechanism might correlate with the intermittent nature of some clinical phenomena and the delayed passage of positive contrast agents through the aqueduct following ventriculostomy in patients with aqueductal stenosis. The notion of a secondary, relative aqueductal stenosis complicating lateral ventricular dilatation has been applied to the adult normal pressure hydrocephalus syndrome.⁶

The clinical presentation of aqueductal stenosis in childhood is well known, and consists of an infant or child with a progressively enlarging head, and with or without the other stigmata of hydrocephalus. In the adult, whose cranial sutures have fused, the hydrocephalus is occult and the diagnosis more difficult. The symptoms and signs in adult aqueductal stenosis have been detailed.^{5,7,9} The clinical picture is varied and non-specific, and while well documented, the symptoms and signs do not fit into a consistent pattern which is readily recognized by the clinician.

Frequent presenting symptoms include headache, loss of memory, and intellectual functions, unsteadiness in walking, vertigo, and seizures. Duration of symptoms prior to diagnosis is more often years than months.^{7,9} The onset is sometimes abrupt, and may correlate with acute decompensation of long-standing asymptomatic hydrocephalus.^{5,8} The headaches have characteristics suggesting increased intracranial pressure. Nausea and vomiting are often associated. The vertigo has no diagnostic features. Both the headache and vertigo may be paroxysmal, and suggest possible intermittent aqueductal obstruction. Seizures include typical generalized major motor and psychomotor episodes, as well as more frequent syncopal-like spells. The mental symptoms have no special features, and may simulate psychogenic disorders or organic dementias. Urinary incontinence and diplopia are less frequent symptoms.

The neurological examination of adults with

aqueductal stenosis similarly reveals non-specific and non-diagnostic findings. The signs are often the same as occur in patients with a posterior fossa tumor. Papilledema and ataxia of gait, with or without cerebellar signs in the limbs, are often present. Nystagmus and pyramidal tract signs may also be found. Spastic weakness of the legs may be the only finding.⁵ Head circumference may be greater than 60 centimeters.⁷

The clinical findings reflect the underlying hydrocephalic process, and are independent of the point of obstruction. There are most commonly no localizing signs that point to the Sylvian aqueduct as the site of the difficulty. Rarely, precisely localizing, eye signs do occur. The Sylvian aqueduct syndrome of Koeber-Salus-Elschnig is a well described combination of neuro-ophthalmological signs consisting of pupillary abnormalities, impaired upward conjugate gaze, convergence and retractor nystagmus, and vertical nystagmus on gaze upward and downward.² Lid retraction and extraocular palsies may be present. The most common cause of this syndrome is neoplasm or vascular infarction in the region of the aqueduct, but the full syndrome or fragments may occur in non-neoplastic aqueductal stenosis.¹¹ Rapid resolution of these eye signs in a patient with aqueductal stenosis after decompression has been described.

Usually, the clinical picture is non-specific and the patient may show little in the way of objective signs. A special problem occurs when the patient does not have significant headache or papilledema. The confusion then is not with a posterior fossa mass. If the mental signs are prominent, the picture might simulate the equally ill-defined syndrome of normal pressure hydrocephalus. The dementia, gait disturbance, and urinary incontinence are features common to both adult aqueductal stenosis and normal pressure hydrocephalus. As a group, the patients with adult aqueductal stenosis are younger. The similarities of these two syndromes of occult hydrocephalus have been discussed as to clinical features and mechanism.⁶

The non-invasive neurological tests including skull films, electroencephalography, echoencephalography, and brain scanning might provide clues as to diagnosis, and may indicate the need for further evaluation in the patient with minimal neurological signs and no papilledema. Unfortunately, these studies are not diagnostic of aqueductal stenosis. Skull x-rays may suggest increased intracranial pressure by demonstrating erosion of the dorsum sellae or prominent convolitional markings. More specific changes of the sellae turcica correlating with a dilated third ventricle have been described.^{4,12} A small posterior fossa might lend more support to the possibility of aqueductal stenosis.⁴ EEG may be normal, show focal spikes, or reveal

diffuse or projected slow activity.⁷ Echoencephalogram may show a dilated third ventricle, although difficulties in interpretation may be considerably increased in the presence of hydrocephalus.⁴ Brain scan is helpful in excluding tumor, and the flow study might suggest enlarged lateral ventricles.

If any of the non-invasive tests are definitely abnormal, considerable benefit is derived since further evaluation to include contrast studies is more clearly indicated. This is of great importance if the patient under consideration does not have papilledema and shows minimal neurological signs. Computerized axial tomography promises to provide a more diagnostic, non-invasive technique. Ventricular size can readily be determined by this technique, and aqueductal stenosis might fall within the diagnostic limits. Contrast studies will, however, no doubt still be needed for confirmation and definition of the aqueductal architecture and dynamics.

The arteriographic features of an enlarged ventricular system are well known and well described.¹² Most helpful are the large sweep of pericallosal artery on the lateral views, and outward bowing and lateral displacement of the thalamostriate vein on the anteroposterior views. Specific angiographic features of the aqueductal stenosis have been delineated.³ Characteristic changes in the course of the precentral cerebellar vein and of branches of the superior cerebellar artery occur. The authors admit that although the angiographic changes are characteristic, air contrast studies are necessary to exclude neoplasm.

Combined ventriculography and pneumography via the lumbar route are the definitive diagnostic procedures in establishing the presence of aqueductal stenosis.¹² Ventriculography defines the lateral ventricles, third ventricle and rostral part of the aqueduct. Pneumography by the lumbar route demonstrates the cisterns, fourth ventricle, and hopefully the caudal part of the aqueduct. Pantopaque ventriculography may be employed as a primary or supplementary procedure.^{4,9,12} Various types of aqueductal configurations have been described, but would seem to have little pathological or therapeutic implication other than the exclusion of tumor.

Early treatments of aqueductal stenosis were in general unsatisfactory and included passage of a tube from the fourth ventricle through the aqueduct to the third ventricle, cerebellar decompression, subtemporal decompression, and various types of third ventriculostomies.⁹ A significant advance in therapy occurred when Torkildsen introduced a technique in which an alternate route for CSF flow was established by passing catheter from one lateral ventricle via a subgaleal tunnel over the occiput to the cisterna magna.¹³ Torkildsen's ventriculocis-

ternostomy is still in use today, and is the preferred technique by some.^{7,9} More recently, ventriculoatrial shunting has been advocated.⁴ Downward displacement of the third ventricle and brain stem are hypothesized as causing changes in the cisterns impairing the circulation of CSF from the cisterna magna to the convexity of the hemispheres. Thus, ventriculocisternal shunting may not provide complete relief of CSF obstruction. Criteria for selection of the best procedure have been proposed,⁴ but are yet to be of established value.

Prognosis with modern treatment is favorable.^{7,9} The majority of adults with aqueductal stenosis improve after a shunting procedure. Many patients are able to return to work.⁷ Visual impairment secondary to chronic papilledema or optic atrophy, and seizures, if present, may persist.^{7,9} Headache, mental symptoms, gait disturbance, and urinary incontinence usually abate.

SUMMARY

A case of adult-onset aqueductal stenosis is presented. The clinical features and the relevant laboratory tests are reviewed. The diagnostic limitations of both the clinical findings and the non-invasive laboratory procedures are emphasized. Computerized axial tomography is predicted to be of considerable value in diagnosis. Definitive contrast studies and treatment are also discussed.

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From the Secretary's Notebook

SUMMARY OF PROCEEDINGS, INTERIM MEETING M.M.A. HOUSE OF DELEGATES, APRIL 12, 1975 AT WATERVILLE, MAINE

The Interim Meeting of the M.M.A. House of Delegates was held at Thayer Hospital in Waterville, Maine on Saturday, April 12, 1975 with an attendance of 47 delegates and alternates and eight guests. John B. Madigan, M.D., President of the M.M.A., called the meeting to order, and George W. Bostwick, M.D., Speaker of the House, presided. Washington and Hancock Counties were not represented at this meeting.

1. **Financial Statement of Income and Expenditure for 1974 and Budget Proposed for 1976** was presented by Dr. Richard C. Leck, Chairman of the Budget Committee. Final action on the proposed budget, and the proposed **increase in dues** for 1976 will take place at the annual meeting of the House of Delegates on Saturday, June 14, 1975 at the Treadway-Samoset Resort in Rockport.

2. The preliminary report of the **Committee on Nominations** was presented by the committee chairman, Dr. Paul A. Fichtner. The report consisted of nominees for vacancies on the standing committees, and two nominees for the office of M.M.A. President-elect, AMA Delegate, AMA Alternate Delegate, and for each position to be filled on the M.M.A. Executive Committee (this year, Districts 2, 4 and 9). A **brief biographical sketch of each officer nominee** was sent to members of the House of Delegates.

Final vote on the report of the Committee on Nominations will take place at the second session of the House of Delegates on Sunday, June 15, 1975.

Dr. Fichtner further stated that the Proposed Changes in the Bylaws, to be voted on in June, will eliminate the necessity of having 2 nominees for each officer vacancy, and the situation of "one running against the other."

3. Committee Reports:

a) *Continuing Education* — Dr. Floyd Goffin, member, was present to answer questions about the CME budget, which was presented to the delegates at the Fall Meeting of the House of Delegates, asking for a decision on whether or not to pay for physician time spent in surveying for accreditation and source of funds for same. A motion was made to approve alternative #1, to pay "physician time at \$150 a day, and \$200 for the team chairman, based

on the assumption that he will spend an additional several hours preparing the survey team report." This was narrowly **defeated**. Several possible alternatives were discussed, and another motion was made that "members serving on survey teams be **reimbursed for their expenses** and for **time spent**, with the provision that monies for this be obtained from the survey hospital, or any other source such as the Board of Registration of Medicine in Maine, insofar as possible." This was **approved**.

b) *Care of the Disadvantaged* — A printed report from the Chairman, John J. Pearson, M.D., was given to each delegate, and it was **accepted**.

c) *Diabetes* — A printed report from the chairman, Melvin Bacon, M.D., was given to each delegate, and it was **accepted**.

d) *Legislation* — The chairman, Brinton T. Darlington, M.D., reported that thus far this session, 120 health-related bills have been printed. He briefly reviewed the status of the more important ones — Medical School for Maine, a bill to authorize the transfer of Board of Registration of Medicine funds for education, and the Optometrist bill.

e) *Mental Health* — John A. Ordway, M.D., Chairman, asked for the M.M.A. to give its support of a position paper of the Council of the Maine Psychiatric Association (dated 2/28/75) in order that the statement can be presented to the American Psychiatric Association in May. Because of the time factor, the delegates approved the temporary suspension of the Rules of Order to act on this, and **voted** to support the position paper which reads:

"Psychologists and psychiatrists have a very different type of training. One of the main differences is that the psychologist has no medical training.

"In general, people who suffer from mental disease do so for many reasons, but essentially the reasons can be classified into two main categories: those people who become mentally ill for emotional reasons and those who suffer from some physical imbalance that causes them to have mental disease. It is also true that many purely physical diseases have many aspects that

appear to be purely emotional but in reality are completely physically based. Mental disease that is purely emotionally based can also ape physical disease.

"Because psychologists lack a medical background, they are unable to make medical diagnoses. As a result, they often will unknowingly treat people with counseling who are badly in need of medical therapy. This results in unnecessary danger to the patient. Only M.D.s and D.O.s are trained to make medical judgments and proper diagnoses. Proper treatment cannot be undertaken without a proper diagnosis.

"Many purely emotional illnesses are often best treated by the use of drugs and other physical treatments. Psychologists are not trained in this area and will often fail to ask for help from medically trained individuals because they are unaware that such therapy is available. This may result in much unnecessary suffering.

"For the above reasons the Maine Psychiatric Association strongly recommends that psychologists should only be allowed to treat mental disease after a definite diagnosis has been made by a physician and that all psychologists must consult with a psychiatrist in regard to these patients."

4. The Executive Committee, as instructed at the last House of Delegates' meeting, reported back on the following:

a) Report of the **Committee on Care of the Disadvantaged**, 12/14/74 — The Exec. Comm. reviewed this report at its 2/1/75 meeting and accepted it for informational purposes. A motion was made and approved that the Committee on Care of the Disadvantaged, in concert with Medical Care Development, Inc., prepare a grant application, if feasible, and the Executive Committee would be happy to consider the application.

b) Cumberland County Medical Society Resolution re **proportionate representation** of membership on the Committee on Health Care Financing — The Exec. Comm. discussed this at its 2/1/75 meeting, and agreed that this would necessitate a change in the bylaws. If Cumberland County so wishes, they may propose such a change to the House of Delegates.

5. **Rules of Order for the House of Delegates** (copy sent to all delegates on 4/1/75) — The Rules of Order, as printed, we **adopted** and are now in force.

6. **Area Designation for the Health Planning Law** — Dr. Manu Chatterjee, Program Coordinator for Maine's Regional Medical Program, was present to explain this new Law which will combine Compre-

hensive Health Planning Agencies, Regional Medical Programs, and experimental delivery care systems all into one. He stressed that this is extremely important legislation. The Governor will be recommending how many health service areas there should be in the State, and the M.M.A. is being asked for their opinion so that it may be transmitted to the Governor. Meetings have recently been held around the State to allow for discussion of the area designations. Arguments for one, or more than one area were discussed by the delegates, and Dr. Chatterjee explained the definition of an area. This A.M. the Executive Committee discussed the Area Designation with Dr. Chatterjee and voted to recommend to the House that they vote in favor of one area for the entire State. Dr. Richard Swengel made a motion that the House of Delegates of the M.M.A. reaffirm the statement of the Executive Committee that the State of Maine be designated as one area, under the Health Planning Law. This was **carried**.

7. **Report of the Bylaws Committee** — Dr. George Bostwick, Chairman, briefly reviewed the proposed amendments (copy sent to all members of the M.M.A. on 4/7/75) and asked that the report be studied and discussed at the county society meetings, and that the delegates bring in recommendations for action on the changes in June.

8. **Report of AMA Delegate** — Dr. Robert E. McAfee reported that no resolutions from the N.E. group are expected this year. Major issues to be discussed at the AMA Convention this year are the malpractice situation, PSRO and the AMA's financial status. If any member has specific instructions for the AMA Delegate, please get in touch directly with Dr. McAfee, or with Dr. Brinton T. Darlington, AMA Alternate Delegate.

9. **Resolution** from York County, asking "that the M.M.A. issue a **legislative newsletter** at appropriate intervals to keep its members informed of State or Federal legislation that may affect the practice of medicine in this State" was read. Dr. Bostwick said it could not be acted upon because the Executive Committee determined that implementation of this would be very expensive, and the resolution did not carry with it the necessary fiscal tag and source of funds. The possibility of printing a newsletter and eliminating the Journal, or alternating a newsletter with an issue of the Journal, was discussed at some length. It was pointed out that a weekly report from the M.M.A. legislative counsel is now sent out to the Executive Committee, Legislative and Government Health Activities Committees, Secretaries and Presidents of the county medical societies, and selected others. This is expensive and time-consuming and the suggestion was

made that if additional members were interested in receiving this weekly report, they send in \$10 and be put on a subscription list. A motion was made that this resolution be referred to the Executive Committee for study and recommendations, and this was **approved**.

10. Other —

a) **Medical School for Maine** — Dr. Charles Hanigan of Lewiston handed out to each delegate an "Historical Perspective on Medical School Education in Maine" and a "University of Maine School of Medicine Proposed Budget Summary." He briefly reviewed the "history" for the delegates and strongly urged physicians and their patients to write to members of the Joint Education Committee of Legislature in support of the bill. Names, addresses and telephone numbers of these committee members were given to all the delegates.

b) A questionnaire being prepared by the State Comprehensive Health Planning Agency, to be used in generating a "**Directory of Primary Care Physicians and Dentists in Maine**" was brought to the delegates' attention, as was decided at the Exec. Comm. meeting this morning. The merits of such a questionnaire were discussed at length, and because of the many objections to some of the questions, Dr. Madigan suggested that the questionnaire be studied for suggested amendments. Dr. Floyd B. Goffin, Consultant for Medical Affairs for SCHPA, who is working on the questionnaire, was agreeable to this approach.

c) Dr. Madigan spoke to the delegates re his concern over many matters confronting the medical profession and stated that the Executive Committee had a special session last night, in addition to today's regularly scheduled meeting, to discuss some of these concerns such as malpractice insurance, and **bargaining unions**. He reported that the California Medical Association recently unanimously approved a commission to study the possibility of becoming a bargaining agent. The M.M.A. Executive Committee discussed the possibility of a Guild of Physicians in Maine to have more clout, at least politically. There is an excellent speaker who is willing to come to Maine to speak about unionism, and Dr. Madigan may ask him to speak at our Annual Session in June.

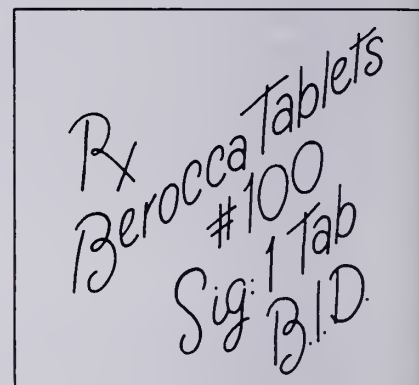
Regarding **malpractice insurance**, Dr. Madigan reported that he and Dr. Francis Kittredge of Bangor attended a session in Washington on this problem, then met in Augusta with the Insurance Supt. of Maine, and our legislative counsel, to discuss plans. While we can't control the cost of mal-

Continued on Page 172

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The Clinical Use of Potassium Supplements

DAVID H. LAWSON, M.D., MRCP

Potassium chloride is widely used in hospital practice. Some 30% of medical inpatients receive this drug either prophylactically or for the correction of hypokalemia.^{1,2} It may be administered parenterally or orally. The parenteral route is usually used when intravenous fluids are required, although this route may also be indicated in the rapid correction of severe hypokalemia following excess loss of potassium-containing fluids from the gastrointestinal or urinary tracts. Either the parenteral or oral route can be used to treat hypokalemia arising as a result of therapy with diuretics,^{3,4} insulin,⁵ laxatives,⁶ or hematinics.⁷ Oral potassium supplementation may be of value in the elderly, particularly those with poor dietary habits.⁸

MEASUREMENT OF POTASSIUM STATUS

The rational use of potassium supplements is complicated by our scant knowledge of the potassium status of individual patients. Usually the only available parameter is the serum (or plasma) potassium concentration. However, less than 0.5% of the total body potassium is present in the plasma and less than 3% is in the extracellular fluid. Moreover, the serum potassium concentration in healthy adults is kept relatively constant within 12% of the mean, whereas total body potassium may vary up to 60% of the mean, depending upon the build of the subject.

As a result the serum potassium concentration may be normal or high in a patient with markedly depleted total body potassium levels. This occurs, for example, in patients with severe diabetic ketoacidosis. Conversely, serum potassium may be low in patients with normal total body potassium levels, as in some patients receiving long-term diuretic therapy. Thus, the serum potassium con-

centration does not necessarily reflect the whole body potassium.⁹

Potassium concentrations alternatively may be measured in erythrocytes, leukocytes, or skeletal muscle cells.¹⁰ Other indicators of potassium status include the exchangeable potassium levels measured following injection of a radioisotope of potassium, or the whole body measurement of a naturally-occurring potassium isotope (⁴⁰K). Unfortunately, these measurements are expensive, not widely available, and yield results which are often difficult to interpret.

Thus, the only measurement routinely available to most clinicians is the serum potassium concentration. This is unfortunate but not entirely useless since the concentration of potassium bathing the myocardial cells and, in particular, the conducting tissues is of vital importance to the normal functioning of these tissues. Serum concentrations of potassium below 2.5 mEq/L or above 6.5 mEq/L may prove fatal irrespective of the total body status at the time. In general, the risks of hypokalemia are less than those of hyperkalemia, except in patients receiving digitalis glycosides in whom hypokalemia is potentially dangerous.¹¹

ORAL POTASSIUM THERAPY

The most common preparations used as potassium supplements are those containing potassium chloride. This compound is preferable to other potassium salts since chloride is required to correct the accompanying alkalosis and to facilitate complete correction of the hypokalemia.^{12,13} Liquid preparations are absorbed directly from the stomach and should be prescribed when rapid replacement by the oral route is necessary.¹⁴ More recently a slow release formulation of potassium chloride (Slow-K) has been marketed in Canada and Europe. This preparation produces less upper gastrointestinal toxicity and avoids the hazard of small bowel ulceration associated with the use of enteric-coated potassium chloride tablets.¹⁵ The biologic availability of potassium chloride in the form of Slow-K is equivalent to that of potassium chloride elixir.¹⁶

The normal daily dietary intake of potassium is approximately 80 to 100 mEq. Slow-K tablets contain approximately 8 mEq of potassium; therefore, 10 Slow-K tablets are required to provide 80 mEq of

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potassium. Such large quantities are not usually needed to prevent potassium depletion. A more usual dose is 24-48 mEq/day (1 or 2 tablets three times a day). On the other hand, doses in excess of 80 mEq/day may be required to correct hypokalemia. Under these circumstances 10% potassium chloride elixir may prove more effective than Slow-K tablets, largely because of its rapid absorption from the stomach. Nevertheless, daily doses of liquid potassium chloride in excess of 100 mEq should be administered with caution because of the possibility of hyperkalemia and gastrointestinal disturbances.²

It is usually assumed that because the commonly used diuretics such as thiazides, furosemide, and ethacrynic acid increase urinary potassium excretion, potassium supplementation is necessary and harmless. This assumption is receiving increasing scrutiny. Several investigators have reported that long-term antihypertensive therapy with diuretics may reduce the serum potassium concentration, but usually only to concentrations above 3.3 mEq/L.¹⁷⁻¹⁹ It is not established whether such patients require long-term potassium supplementation. Schwartz and Swartz²⁰ found that patients with thiazide-induced hypokalemia require 60 mEq of potassium per day to correct the deficit. Nevertheless, the mean potassium concentration in their "hypokalemic" patients was 3.8 mEq/L — within the usual normal range. They also found that the urinary excretion of potassium increased with the amount of potassium consumed. Their data did not indicate that potassium supplements were either being retained or even were necessary.

There are few studies of total body potassium levels during long-term diuretic therapy of edema. The limited data suggest that not all subjects will retain the administered potassium,²¹ but further studies are needed before definitive conclusions can be drawn.

Most practicing physicians prescribe additions of 40 to 50 mEq of potassium to the daily diet of patients taking potassium-losing diuretics, irrespective of the indication for the diuretics. However, many such patients do not need additional potassium, and in some it may be harmful. As an alternative to potassium supplements, some have adopted the concurrent use of potassium-retaining diuretics, such as triamterene or spironolactone. The use of such drugs carries the hazard of hyperkalemia particularly when potassium supplements are coadministered.²²

INTRAVENOUS POTASSIUM THERAPY

In patients with normal renal function, potassium chloride is commonly added to infusion bottles in a concentration of 40 mEq/L. Infusion rates generally should not exceed 10 mEq per hour or 120 mEq per

day. Potassium chloride should not be added to certain fluids such as mannitol, blood or blood products, and amino acid- or lipid-containing solutions since it may precipitate some of these substances from solution or cause lysis of infused red blood cells. Potassium chloride can be added to most other intravenous solutions. Care is required when making the addition, particularly to non-rigid containers. If potassium is added to an upright container, pooling may take place resulting in locally high potassium concentrations. Infusion of such solutions has caused fatal hyperkalemia.²³⁻²⁴

Rapid potassium replacement is needed in certain clinical situations, such as during the diuretic phase of acute renal failure, or early in the course of diabetic ketoacidosis. Such patients are usually acidotic, depleted of total body potassium, and experiencing considerable urinary loss of potassium. Serum potassium levels, however, may be misleadingly normal or even high because of the systemic acidosis. To prevent hypokalemia, rapid replacement of potassium is needed concurrent with correction of acidosis. Nevertheless, the rate of infusion should not be so rapid as to produce hyperkalemia. Repeated estimations of plasma potassium concentrations are necessary in these patients, who may be given potassium in concentrations of 40 mEq/L in several consecutive liters of fluid,²⁵ or in even higher concentrations (up to 60 to 80 mEq/L) for brief periods.²⁶ Even with adequate biochemical back-up, the electrocardiogram should be monitored in all patients receiving intravenous potassium at rates exceeding 20 mEq per hour for periods exceeding 2 hours. Peaking of the T-wave or loss of R-wave amplitude indicates that the rate of potassium infusion is excessive and should be reduced.²⁷ These electrocardiographic changes must be interpreted in light of the blood pH and should be rapidly verified by measurement of serum potassium concentrations.^{28,29}

INTRAPERITONEAL POTASSIUM ADMINISTRATION

Potassium is usually added in low concentrations to peritoneal dialysis fluid in order to correct hyperkalemia associated with renal insufficiency. Peritoneal dialysis can also be used to treat severe refractory congestive cardiac failure³⁰ or acute pulmonary edema.³¹ In these patients the dialysate potassium concentration is set at 4 mEq/L. There is no reason why peritoneal dialysis could not also be used to treat hypokalemia. This might apply to patients with congestive heart failure receiving digoxin and diuretics, in whom digitalis toxicity precludes oral potassium administration, and an intravenous fluid load is undesirable. Such patients should respond to peritoneal dialysis using "high" concentrations of potassium (4 mEq/L in the dialysis fluid) and alternating the dialysis glucose

concentration (between levels of 1.5 and 5%). This will result in rapid removal of excess fluid, correction of the potassium deficit, and alleviation of the symptoms of digoxin toxicity.

HAZARDS OF POTASSIUM SUPPLEMENTS

In a recent review of data from the Boston Collaborative Drug Surveillance Program, almost 6% of 4,900 consecutive recipients of potassium chloride experienced one or more undesired effects of the therapy.² Hyperkalemia was the most common adverse effect; it occurred in 3.6% of recipients. Hyperkalemia was more common in the elderly, in those with pre-existing uremia, and in those who received the drug both orally and intravenously. Of the 4,900 recipients, 7 died in part as a result of hyperkalemia; in a further 21, the serum potassium levels were sufficiently high to be life-threatening. Other side effects such as gastrointestinal disturbances occurred much less frequently and did not appear to be of major significance. In another study from the same program, Greenblatt and Koch-Weser²² reported that hyperkalemia was three times more common in spironolactone recipients who also received potassium chloride than in those who did not.

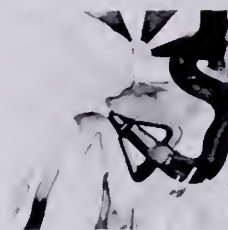
Adverse reaction rates following Slow-K administration probably are similar to those associated with liquid potassium preparations, but no adequate comparative data are available. Enteric-coated potassium chloride tablets are more toxic and are being prescribed less frequently because a considerable number of patients develop small bowel ulceration due to locally high concentrations of potassium.^{15,16,32,33}

CONCLUSIONS

In 1974 Burchell³⁴ suggested that "a debate be staged with the title: Resolved: That more lives have been lost than saved by potassium therapy in the past year in American hospitals." Published data from the Boston Collaborative Drug Surveillance Program lend some support to this notion; although deaths from hyperkalemia attributed to potassium therapy have been reported,^{2,22,35} no deaths from diuretic-induced hypokalemia have been observed. Furthermore, there is considerable variability in the extent of potassium administration to medical inpatients, suggesting that less prolific use of these drugs might result in less toxicity without increasing the prevalence of hypokalemia.

The risk of hyperkalemia during outpatient use is unknown, and may be less than the hazard of hypokalemia. Fewer patients are admitted with hyperkalemia resulting from excessive potassium supplementation than are admitted with diuretic-induced hypokalemia. However, potassium-

Continued on Page 169



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makes sense in edema*.

Neither inconvenient, unpalatable, expensive potassium supplements nor special K⁺ rich diets are needed as a rule. Just 'Dyazide' once or twice daily for control of edema.

Serum K⁺ and BUN should be checked periodically (see Warnings section).

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Indications: *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—

both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy

patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F Co., Carolina, P.R. 00630
Subsidiary of SmithKline Corporation

'Dyazide' gets excess water and salt out and helps keep essential potassium in.





Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

- Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
- Can relieve nausea and vomiting often associated with vertigo*.
- Usual adult dosage for Antivert/25 for vertigo*: one tablet t.i.d.
- Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
- Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG 
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert[®]/25 (meclizine HCl) 25 mg. Tablets for vertigo*

PAIN RELIEF FOR THE MAJORITY

NO.4—for pain intensity below the need for injectables

As a rule, only pain that requires morphine is beyond the scope of Empirin® Compound with Codeine No. 4. That's because it delivers a full grain of codeine. (In the preferred phosphate form.) Its antitussive action is particularly appreciated by patients with fractured ribs, and following chest or abdominal surgery. Its low addiction liability is a bonus for all patients who require potent analgesia.

NO.3—for almost all other kinds of lesser pain

Most other kinds of lesser pain respond to Empirin Compound with Codeine No. 3—whether musculoskeletal, neurological, soft-tissue or visceral. One might say No. 3 is an "all-purpose" analgesic — not too little, not too much. Just right for your out-patients in these categories.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

BURNS

Wherever it hurts
EMPIRIN® COMPOUND 2 CODEINE

No.3, codeine phosphate* (32.4 mg) gr ½ • No.4, codeine phosphate* (64.8 mg) gr 1

*Warning — may be habit-forming.

Each tablet also contains aspirin gr 3½, phenacetin gr 2½, caffeine gr ½.

induced hyperkalemia may cause sudden fatal arrhythmias which could preclude hospitalization of such patients.

Uncritical use of potassium chloride unfortunately has become commonplace. Increasing recognition of the potential hazards of potassium indicates a need for a more rational approach to potassium therapy. Great care is required in the use of intravenous potassium, particularly when it is added to non-rigid infusion sets. When large quantities must be given parenterally, and intravenous fluids are contraindicated, potassium replacement by the intraperitoneal route during peritoneal dialysis seems to be a reasonable alternative which deserves further study.

Oral potassium supplementation may not be required in all patients who receive diuretic therapy, providing adequate dietary intake is established. Potassium supplements are needed most by patients receiving long-term therapy with potassium-losing diuretics who are also receiving digoxin or have established liver disease. In general, potassium chloride should be given orally for prophylaxis against potassium depletion and for the treatment of hypokalemia unless the latter is severe (serum concentration of less than 2.5 mEq/L), of recent onset, or associated with severe gastrointestinal disturbances.

ACKNOWLEDGEMENT

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DEAN H. FISHER, M.D.
COMMISSIONER

State of Maine

Department of Health and Welfare

THE ROLE OF THE PHYSICIAN'S ASSISTANT

RICHARD H. WILLARD*

An ancient sage was once asked by a troubled young man who wanted to plan for his future, "In these changing times, what can I rely upon to endure?" The sage furrowed his brow, rested his chin upon his hand, and after much thought replied, "change." He explained, "Of all things which men hold true, they may rely on only change to endure."

The medical profession has seen more clearly than most how accurate the sage's observation has been. In the rapidly changing socio-economic conditions of our times, the medical profession has responded in many ways to meet the changing expectations placed on it. Perhaps one of the most unique responses has been the development of the highly-trained Physician's Assistant.

Since the first experimental Physician's Assistant program started in 1965 at Duke University Medical Center, more than 1,600 P.A.'s have graduated from 40 American Medical Association-approved courses across the nation. More than half are involved in delivering primary health care to rural areas such as Maine. Peter J. Leadley, M.D., Director of the Bureau of Health, Maine Department of Health and Welfare calls the P.A. program, "another example of the medical profession responding to the challenge of extending quality health care to more people in rural areas."

The P.A.'s function is to relieve much of physician's routine workload which does not require extensive medical training. His training enables him to:

1. Take patient histories and record other patient data.
2. Carry out screening types of routine and special examinations.
3. Do assigned ward work of the physician.
4. Make hospital and nursing home rounds as requested by the physician.
5. Render or assist in first aid in the hospital emergency room or elsewhere.
6. Order laboratory studies, x-ray examinations, etc., as directed by the physician.



Robert Girard, Physician's Assistant, taking patient history.

7. Assist the surgeon in the operating room, cast room and elsewhere.
8. Give research assistance as outlined by the physician.
9. Supervise administrative work which may require medical insight.
10. Do certain technical procedures in the absence of a technician.
11. Conduct educational programs such as teaching aides, etc.
12. Instruct patients in their home-care procedures.
13. Carry out such other clinical and research procedures as the assistant's innate ability, plus his education and training permit to undertake under the guidance of the physician.

Hu C. Myers, M.D. of the Broadus Hospital and Myers Clinic in West Virginia, writing in the Maryland State Medical Journal, estimates the P.A. can relieve the physician of at least 30% of his routine work. He says this allows the doctor to direct more of his time and special skills towards diagnosing and curing patients.

Maine currently has 21 Physician's Assistants qualified and registered by the Maine Board of Medical Examiners. Robert Girard, at the Rumford

*Publicity Representative I, Office of Information and Education, Department of Health and Welfare.



Robert Girard, Physician's Assistant, cutting away a leg cast.



Removal of leg cast, a procedure that may be handled by a Physician's Assistant.



Robert Girard, Physician's Assistant, assisting a doctor with minor surgery in the ER.



A Physician's Assistant assists the surgeon in the operating room.

Community Hospital, is one of them.

Girard had been a hospital corpsman in the Military for 11 years when he decided on a civilian career as a P.A. He trained at the Dartmouth College's Medical School, where competition was intense. He was one of 2,000 applicants accepted for his class of 25.

Girard chose to pursue his career in Maine, as in his travel around the world, he picked Maine as the place he most likes, and feels is the best place to raise his family. In his choice of Maine, he is also helping the State with its need for more professional health care providers.

Statistics from the State Health Information Project, operated on a grant from the Maine Department of Health and Welfare, show that Maine has a lower doctor to population ratio than the rest of the nation. Nationwide the average number of doctors servicing 10,000 people is 11.6. In Maine there are 9.8 doctors for each 10,000 people. Vermont has a ratio of 15.4 and New Hampshire has 12.1.

Girard received help in getting his position in Rumford from the MEDIHC (military experience directed into Health Careers) Program, a joint effort of the Maine Department of Health and Welfare and the Maine Department of Manpower Affairs. This program is aimed at encouraging former service men and women with medical training to continue in the medical field and in Maine. Girard heard of the program while still in the service. When he contacted the MEDIHC Program, through the Sanford Employment Office, his name and qualifications were circulated around the State. Through this help, an interview was arranged with the Rumford Hospital, which needed someone with his qualifications.

For the past three months, he has been working at the hospital to acquaint himself with the special skills of each doctor on the staff and to familiarize himself with the resources available at the hospital.

He is scheduled to work with a clinic soon to open in Bethel, an area now underserved in the health field.

"The rural doctor is traditionally overworked," Girard observes. "As a Physician's Assistant I can lighten his workload, making him available to give the people the more expert care they need."

Before coming to Rumford, he worked under the supervision of a doctor in rural northeastern Maine. He found that sometimes a patient's problems were emotional as well as physical. Because of the enormous demand on the Physician's time, he was not always able to get at the root of the problem and had to treat only the physical symptoms. Girard wants to become involved with assisting the doctor to treat the entire patient. He feels that his work as a supplement to the doctor will enable the entire patient needs to be more effectively treated.

To date, the Physician's Assistants have been accepted by patients. But patient acceptance is tied to another, potentially more troublesome problem . . . the possibility of malpractice suits. This fear had caused some physicians to shy away from using the P.A. in the past. The latest signs indicate that this is becoming less of a problem. The P.A. malpractice insurance is attached to the doctor's policy, as is that of an office nurse. Thus, the P.A. is liable for his own acts, although the ultimate responsibility is borne by the doctor who bears responsibility for all services under his practice.

Physicians involved with P.A.'s feel that they will

actually help to reduce the number of malpractice suits and the presence of the P.A. will improve the quality of health care.

To date, results appear to sustain this viewpoint. Last year, after the Physician's Assistant had been in existence for nine years, there were two malpractice suits filed against the P.A.'s and their sponsoring physicians nationwide. Both suits were dismissed before reaching court.

"One thing a Physician's Assistant must have," Mr. Girard stressed, "is the ability to know his own limitations. When the P.A. finds something abnormal or something he is unsure of, he brings it to the doctor's attention. That's what our job is all about."

The Maine MEDIHC Program, which assisted in placing Robert Girard in Rumford, has many more P.A.'s and other people with medical specialties ready to meet the needs of Maine hospitals and communities.

Robert Emerson, MEDIHC Co-ordinator for the Maine Department of Manpower Affairs, says he has extensive listing of health personnel such as laboratory technicians, operating room technicians, etc., available to meet demand. "Last year," he says, "MEDIHC also assisted in placing a hospital administrator in Southern Maine. For hospitals and clinics needing trained personnel, help is as far away as their nearest local employment office."

FROM THE SECRETARY'S NOTEBOOK — *Continued from Page 164*

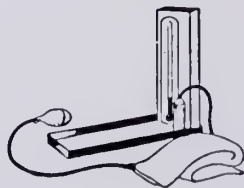
practice insurance now, our current course is to try to obtain insurance for all.

d) Dr. Bostwick, Speaker of the House of Delegates, announced that the following physicians will be serving on Reference Committees for the June meeting: Drs. Raymond E. Culver, Eric F. Nicholas, Robert W. Agan, Anthony J. Horstman, Hayes

G. Bowne, Charles A. Hannigan, Jou S. Tchao, John A. Woodcock and O. Thomas Feagin.

11. Adjourned at 5:45 P.M.

PATRICIA A. BERGERON
Secretary-Treasurer, M.M.A.



Maybe the patient's self-diagnosis is right. He could have hay fever. But that bright red nasal mucosa, along with the thick discharge and excoriation around the nares, strongly suggests that the main problem is a cold. Hay fever or another form of allergic rhinitis may or may not be an underlying factor.

If a complete history and examination rule out allergic rhinitis, the long-term outlook will be a lot more favorable than his own "diagnosis" would have indicated.

But right now, whether he's got allergic rhinitis or a cold, he's suffering from the same irritat-

ing symptoms of drip, congestion and stuffiness. Try DIMETAPP EXTENTABS®. They're formulated to relieve these symptoms without much chance of causing drowsiness or overstimulation. Your patients will appreciate the 24-hour relief they can get from just one tablet every 12 hours.

Cold or



Allergy?

Whether it's a cold or an allergy, Dimetapp Extentabs® effectively relieve stuffiness, drip and congestion.

INDICATIONS: Dimetapp Extentabs are indicated for symptomatic relief of allergic manifestations of upper respiratory illnesses such as the common cold, seasonal allergies, sinusitis, rhinitis, conjunctivitis and otitis. In these cases it quickly reduces inflammatory edema, nasal congestion and excessive upper respiratory secretions, thereby affording relief from nasal stuffiness and postnasal drip.

CONTRAINDICATIONS. Hypersensitivity to antihistamines of the same chemical class. Dimetapp Extentabs are contraindicated during pregnancy and in children under 12 years of age. Because of its drying and thickening effect on the lower respiratory secretions, Dimetapp is not recommended in the treatment of bronchial asthma. Also, Dimetapp Extentabs are contraindicated in concurrent MAO inhibitor therapy.

WARNINGS: Use in children. In infants

and children particularly, antihistamines in overdosage may produce convulsions and death.

PRECAUTIONS: Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. Until the patient's response has been determined, he should be cautioned against engaging in operations requiring alertness such as driving an automobile, operating machinery, etc. Patients receiving antihistamines should be warned against possible additive effects with CNS depressants

such as alcohol, hypnotics, sedatives, tranquilizers, etc.

ADVERSE REACTIONS: Adverse reactions to Dimetapp Extentabs may include hypersensitivity reactions such as rash, urticaria, leukopenia, agranulocytosis, and thrombocytopenia; drowsiness, lassitude, giddiness, dryness of the mucous membranes, tightness of the chest, thickening of bronchial secretions; urinary frequency and dysuria, palpitation, hypotension/hypertension, headache, faintness, dizziness, tinnitus, incoordination, visual disturbances, mydriasis, CNS-depressant and (less often) stimulant effect, anorexia, nausea, vomiting, diarrhea, constipation, and epigastric distress.

HOW SUPPLIED: Light blue Extentabs in bottles of 100 and 500.

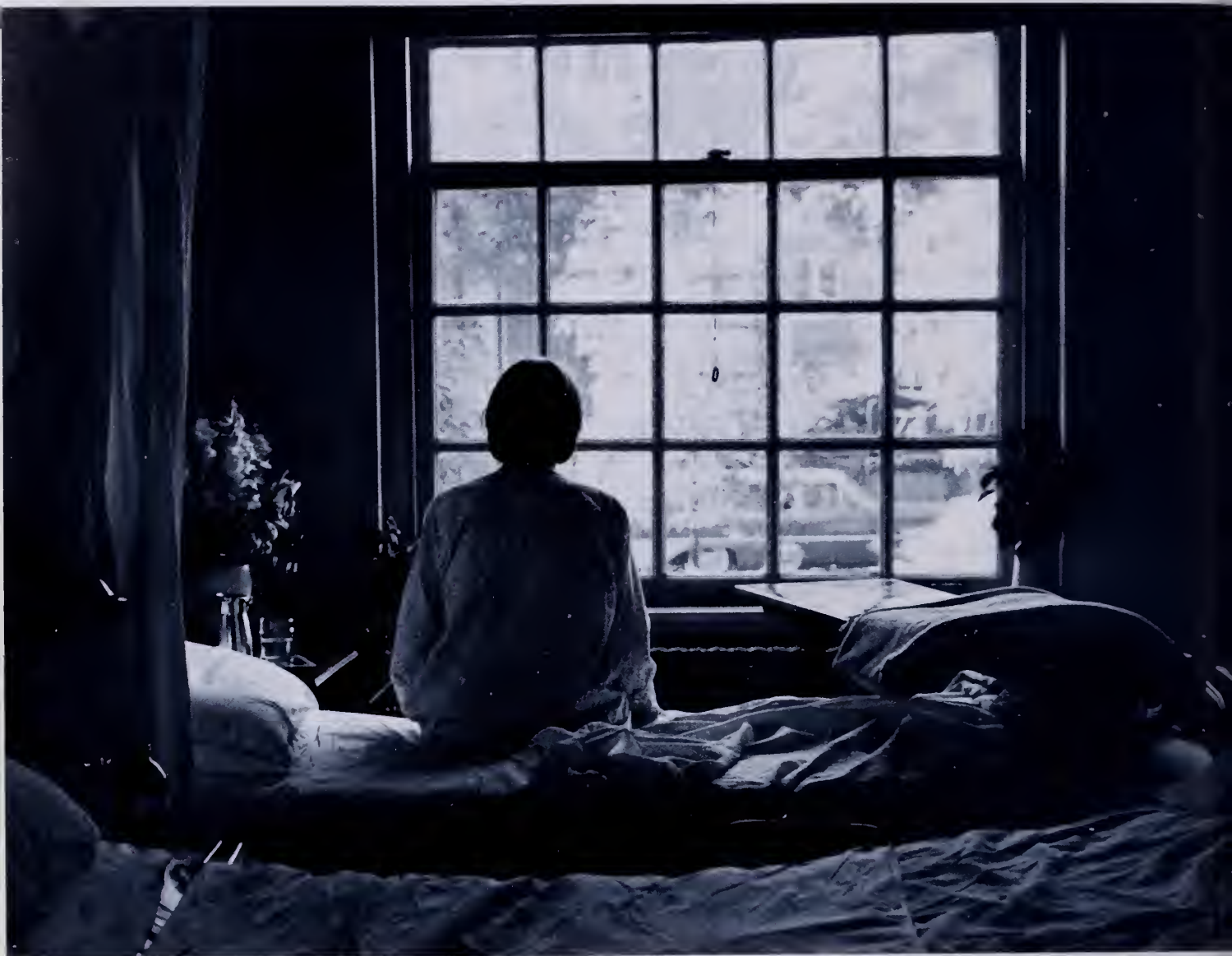
Dimetapp Extentabs®

Dimetane® (brompheniramine maleate), 12 mg.; phenylephrine HCl, 15 mg.; phenylpropanolamine HCl, 15 mg.

A-H-ROBINS

A. H. Robins Company, Richmond, Va. 23220

when pain goes on... and on... and on—



For the patient with a terminal illness, PAIN past, present, and future can dominate his thoughts until it becomes almost an obsession. The more he is aware of the pain he is now experiencing, the more difficult it is to erase his memory of yesterday's pain, and to allay his fearful anticipation of tomorrow's pain.

Surely the last thing this patient needs is an analgesic containing caffeine to stimulate the senses and heighten pain awareness. A far more logical choice is Phenaphen with Codeine. The sensible formula provides $\frac{1}{4}$ grain of phenobarbital to take the nervous "edge" off, so the rest of the formula can help control the pain more effectively. Don't you agree, Doctor, that psychic distress is an important factor in most of your terminal and long-term convalescent patients?

the analgesic formula that calms instead of caffeinates

Phenaphen[®] with Codeine

Phenaphen with Codeine No. 2, 3, or 4 contains: Phenobarbital ($\frac{1}{4}$ gr.), 16.2 mg. (warning: may be habit forming); Aspirin ($2\frac{1}{2}$ gr.), 162.0 mg.; Phenacetin (3 gr.), 194.0 mg.; Codeine phosphate, $\frac{1}{4}$ gr. (No. 2), $\frac{1}{2}$ gr. (No. 3) or 1 gr. (No. 4) (warning: may be habit forming).

Indications: Provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products, excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.

Phenaphen with Codeine is now classified in Schedule III, Controlled Substances Act of 1970. Available on written or oral prescription and may be refilled 5 times within 6 months, unless restricted by state law.

A. H. Robins Company, Richmond, Va. **A-H ROBINS**



Maine Blue Cross and Blue Shield News

10 NEW BOARD MEMBERS ELECTED

The election of 10 new board members and a vote to change the board structure marked the April Maine Blue Cross and Blue Shield Annual Meeting held in Portland.

Newly elected to represent subscribers on the Board were Doris D. Karter, Personnel Services Manager for Scott Paper Company; John Parker, Controller of Bath Iron Works; and Constantine Karvonides, Vice President of Pepperell Trust Company. Re-elected to represent subscribers on the Board were John W. Jackson, Controller of the Hanold Company, and Benjamin J. Dorsky, President of the Maine State Federated Labor Council.

Elected for their first terms representing participating providers were Fletcher H. Bingham, Ph.D., President of the Maine Hospital Association, and Laurier T. Raymond, Jr., a trustee of St. Mary's Hospital. Re-elected to represent providers were Warren C. Kessler, Executive Director of Augusta General Hospital; George W. Avery, Administrator of James A. Taylor Osteopathic Hospital; and Eugene E. Loubier, Administrative Director of Special Projects at the Maine Medical Center.

Professionals elected for their first terms representing their peers were Harold F. Knuuti, M.D., Belfast; George W. Wood, III, M.D., Bangor; Parker Mann, D.M.D., Auburn; Lewis N. Estabrooks, D.M.D., South Portland; and John R. Davy, M.D., Portland. Re-elected to the Board was Michael A. Longo, D.O., Bangor.

The Maine Blue Cross and Blue Shield Board, which had numbered 24 with 8 subscriber members, 8 hospital members, and 8 professional members, was restructured to total 31 members. With this change in the corporate bylaws, eleven Board members represent the subscribing public, five are salaried employees of member providers, five non-salaried board members of member providers, and ten are professionals.

In the reports of the officers of the corporation, major expansions in benefits, members, and numbers of claims were noted despite depressed economic conditions in 1974. Commenting on Key 1974 statistics, Richard F. Nellson, President of Maine Blue Cross and Blue Shield, stated that membership had exceeded the 475,000 mark by year-end, and a total of 669,879 Blue Cross and Blue Shield claims amounting to \$46,207,589 were submitted during 1974. He also noted that four major benefit expansions had been put into effect in 1974, including the major Blue Cross out-patient hospital laboratory pilot program instituted last fall to provide full coverage for diagnostic laboratory services when indicated as being necessary by symptoms of illness or injury.

George Baer Connard, Chairman of the Maine Blue Cross and Blue Shield Board of Directors, explained in his annual message that: "Instead of subscribers dropping their coverage under trying conditions, we found most subscribers keeping it, seeing it as a necessity of life. It was interesting to note that fewer members cancelled in 1974, a year of economic crisis, than in the previous year. In fact, we actually experienced a higher than normal increase in enrollment. Although not many Maine Blue Cross groups experienced heavy lay-offs, many of those subscribers who found themselves without group coverage switched to non-group contracts."

Connard concluded: "In the face of the myriad challenges thrown up to us in 1974, we survived in a healthier state than before. Economic turbulence brought an already financial responsible corporation into a more stringent belt-tightening mode, and this effort will certainly be strengthened throughout 1975. It was satisfying to know that our planning efforts, and our programs to help bring about more efficient use of healthcare facilities, were effective and will guide us through uncertain times. These efforts will continually be built upon in 1975."

County Society Notes

Penobscot

The monthly meeting of the Penobscot County Medical Society was held on January 21, 1975 at the Pilot's Grill, Bangor, Maine.

The meeting was opened by the President, Dr. David M. Sensenig.

Mr. Ralph Osgood, a representative of Blue Cross and Blue Shield was present at the meeting to discuss the new 80 percent UCR contract which has gone into effect this past year. He discussed the origin and background of the 80 percent UCR contract and the reasons for and the basis upon which it was devised. In addition to his discussion concerning this plan, he also discussed out-patient benefits under Blue Cross. Following his presentation, a question and answer session followed.

The business portion of the meeting was opened with the reading of the minutes of the December 1974 meeting. These minutes were approved as read.

The application of Dr. Paul H. LaMarche was submitted to the membership for their consideration after first having been reviewed and approved by the Executive Council. The application of Dr. LaMarche was unanimously approved.

A discussion concerning the 80 percent Blue Cross-Blue Shield contract was then held. After a rather thorough discussion of this topic, a motion was made by Dr. Hadley Parrot, which was subsequently seconded and passed, to request guidance and recommendations from the Committee on Health Care Financing of the Maine Medical Association in order that we may formulate our own position on the 80 percent UCR contract.

Dr. Charles D. McEvoy, Jr. moved and it was seconded and passed that an informed representative, knowledgeable in the health care in the Province of Nova Scotia, be invited to speak at a future meeting of the Society in order to discuss the topic of provincial health insurance, and how it is applied in the Province of Nova Scotia.

As there was no future business, the meeting was then adjourned.

The monthly meeting of the Penobscot County Medical Society was held at the Red Lion Restaurant in Bangor, Maine on February 18, 1975.

Following a social hour and dinner, the meeting was opened by the President, Dr. David M. Sensenig.

The scientific portion of the meeting was presented by Dr. Albert Dibbins, Pediatric Surgeon from the Maine Medical Center in Portland, Maine. His topic "New Approaches to Common Pediatric Surgical Problems" was a most interesting presentation and discussion of numerous pediatric problems requiring surgical intervention for their management and correction. Following the presentation with Dr. Dibbins, a discussion and answer session followed. Following the scientific presentation, the business portion of the meeting was then begun. The minutes of the January 1975 meeting were read and approved as amended.

Under old business, Dr. Thomas L. Watt made several comments and observations regarding the Blue Cross-Blue Shield 80 percent UCR contract. Dr. Watt raised several questions about this contract and the reasons or motives for its establishment. Dr. Watt presented the following motions:

1. That the President or Secretary contact Blue Shield to express our displeasure of the 80 percent Blue Shield UCR contract and suggest that we, as a County Society, would consider withdrawal from participation in Blue Shield if such contract was not withdrawn or amended.

2. That the President or Secretary contact other county societies and express our displeasure with the contract and enlist the support and encourage other societies to express their displeasure likewise.

Under discussion, Dr. Watt was particularly concerned that Blue Shield was entering into the contraction of physician services without the physician's consent to such contractual agreement. Dr. George W. Wood, III made a motion to table the motions of Dr. Watt. Dr. Wood's motion to table was seconded and passed. Dr. Watt moved, and it was seconded and defeated, that the membership be told as to their approval and disapproval as to the 80 percent UCR contract.

Under new business, the application of membership in the Penobscot County Medical Society of Dr. Franklin Blackmer was presented and unanimously approved by the Society.

Dr. Lewis E. Phillips made a motion, and it was seconded and passed, that a future meeting of the Penobscot County Medical Society would be devoted to additional discussion of the 80 percent Blue Shield UCR contract.

Dr. Charles D. McEvoy, Jr. made a motion, and it was seconded and passed, that the Penobscot County Medical Society express publicly their support for the University of Maine School of Medicine and seek publicity in news releases, as well as direct contact with legislators in an effort to obtain their support for such a school. This action was contingent upon demonstration through a review of the minutes of the County Society, that the Society is on record as being in support of the Medical School.

Dr. John A. Woodcock made a motion, and it was seconded and passed, that the President appoint an Ad Hoc Committee consisting of representatives of the County Medical Society to join with similar representatives from the County Bar Association in the time questions of medical-legal interest and to maintain a meaningful line of communication between the two organizations.

As there was no further business, the meeting was adjourned.

The monthly meeting of the Penobscot County Medical Society was held on March 18, 1975 at the Ramada Inn.

The meeting was opened by the President, Dr. David M. Sensenig who then introduced the speaker for the evening, Dr. John Hutchinson, Associate Professor of Clinical Surgery, Columbia University, who discussed newer techniques of coronary artery surgery. Dr. Hutchinson presented information relevant to his experience in coronary artery surgery and presented survival data and long-term follow-up data with regard to his patients. Following an interesting discussion and slide presentation, a question and answer session followed.

Following the scientific presentation, the business portion of the meeting was held.

The minutes of the February 1975 meeting were approved as read.

Old Business — Dr. Sensenig appointed the Ad Hoc Committee for Medical-Legal Affairs in cooperation with the Penobscot County Bar Association, as directed by the membership at the February 1975 meeting. Those members appointed to this committee included Drs. John Woodcock, Warren G. Strout and David Sensenig.

New Business — An announcement was made concerning the development of Public Law 93-641, the National Health Planning and Resources Development Act of 1974. Under this act, there will be the establishment of State Health Planning and Development Agencies and Local Health Systems Agencies. The new program would replace the Comprehensive Health Planning, Regional Medical Program and the Health Facilities Planning and Construction Program. Regional meetings are being held throughout the State in order to obtain input from local and regional areas regarding the designation or division of the State into regional agencies for the implementation of this program. The attendance at one or more of these planning sessions was encouraged. It was emphasized that in the future this organization or agency will become the primary agency which will deter-

mine health planning within this State.

Dr. Charles D. McEvoy, Jr. made a motion, and it was seconded and passed, that the Penobscot County Medical Society go on record as favoring the development of a Medical School for the State of Maine. In addition, it was moved, seconded, and passed that a letter be sent to Senator Bennett Katz, Chairman of the House-Senate Education Committee, informing him of our support for the medical school.

Dr. Franklin E. Bragg, II made a motion, and it was seconded and passed, that a letter be sent to Governor James Longley expressing our support for Public Law 93-641, the National Health Planning and Resources Development Act, and offering our support and cooperation in the implementation in the local Health Systems Agencies.

As there was no further business, the meeting was adjourned.

PHILIP G. HUNTER, M.D., *Secretary*

Androscoggin

The Androscoggin County Medical Association convened at its monthly meeting on March 20, 1975 at Steckino's Restaurant, Lewiston, Maine, with 32 members present.

The minutes of the previous meeting were read and approved.

The Secretary read a letter of correspondence from the Senior Medical Consultants of Maine indicating their wish to provide consulting service as may be indicated. This will be taken into consideration by the Program Committee for possible future use.

Membership was reminded that the Interim Meeting of the House of Delegates of the Maine Medical Association will be held at Thayer Hospital on Saturday, April 12, 1975.

Membership was appraised of the proposed budget for the continuing medical education accreditation program.

Since our Executive Committee member could not be present for the meeting, a summary of the Minutes of the Executive Committee meeting of the Maine Medical Association of February 1, 1975, was reviewed with the membership.

A letter to Dr. Daniel F. D. Russell of Leeds, Maine was read to the membership indicating the honor to be bestowed upon him at the Annual Meeting of the M.M.A. at the Treadway-Samoset in June. Dr. Russell has been in practice for 70 years. A delegation from the County Medical Association will assist Dr. Russell as is necessary for transportation, etc.

Copy of the Maine Medical Association's Committee on Ethics and Discipline procedure was reviewed with the Committee and referred to Dr. Thomas F. Shields, to be incorporated in the revision of the County Medical Association's Constitution and Bylaws.

Minutes of the meeting of Peer Review for Ethics and Grievances held on March 10, 1975 were reviewed with the membership.

The Public Relations Committee had attempted to prepare a position paper for the County Medical Association to be forwarded on to Representative Rostenkowski (Democrat-Illinois) who is Chairman of the Subcommittee on Health of the Committee of Ways and Means for presentation to that Committee's National Health Insurance Advisory Panel. It was determined that a single letter could not represent all the views of the medical community in this region. The membership is invited to provide their own individual letters as they feel inclined.

Copy of a letter forwarded to the Maine Medical Association from the Medical Nursing Staff at Pineland Center was read and forwarded on to Dr. Russell A. Morissette, member of the Board of Visitors of that institution.

Under old business, the previously-tabled report on medical liability and the two resolutions before the chair were once again discussed. By unanimous vote, the two resolutions are forwarded on to the Maine Medical Association. These resolutions are not for adoption by the House of Delegates but are intended as a direct instruction from the members of Androscoggin County to its parent organization, the Maine Medical Association, to aid in resolution of increasing problems of medical liability and corresponding liability insurance. The membership was

also advised that Mr. Hogarty, Insurance Commissioner for the State of Maine, had provided us with a copy of the filing memorandum from Aetna Insurance Company which was the actuarial base for their premium increase in 1974. Membership is most appreciative of the cooperativeness and rapid response from Mr. Hogarty's office following a letter from Dr. Paul M. Beegel.

Dr. Philip L. Archambault had correspondence with The Honorable William S. Cohen, Representative, Second District of Maine, about this medical liability problem. Representative Cohen forwarded a position paper entitled "The Medical Malpractice Insurance Crisis" prepared by the House Wednesday Group, dated January 29, 1975. This position paper was reviewed for the membership.

Under new business, the necrology for Dr. James A. Williams was read to the membership. Upon command of the President, his necrology will be spread upon the records of the Androscoggin County Medical Association, the Maine Medical Association, and a copy forwarded to Dr. Williams' widow, Mrs. Alice B. Williams of Mechanic Falls, Maine.

RICHARD M. SWENGEI, M.D., *Secretary*

Washington

The regular meeting of the Washington County Medical Society was held on March 31, 1975 at the Peavey Memorial Library, Eastport, Maine, with eight members and guests present.

The meeting opened under the direction of Dr. G. Bernard Shaw, President of the Society, Machias, Maine.

I. Minutes of last meeting read and approved.

II. Discussion as to obtaining services of an Executive Secretary for the Washington County Medical Society, who would coordinate all the activities; not only of the Society but of the various Para-medical groups working in the County. Dr. James C. Bates, who is a member of the committee to look into this matter, felt that we were unable at present to give funding from our own resources, plus Federal funds. He recommended that we drop this matter at present, and it was so voted.

III. Dr. Christopher D. Mace, Machias, Maine has applied for membership in the Washington County Medical Society. It was moved, seconded and passed that Dr. Mace be elected a member of the Washington County Medical Society.

IV. Members of the Bylaws Committee, appointed by Dr. G. Bernard Shaw, including himself, plus Drs. John Kazutow, Columbia Falls, Maine and Carl K. Aselton, Jr. of Cherryfield, Maine; each were given copies of the old Washington County Medical Society Bylaws, plus a copy of the recently revised Bylaws of the Cumberland County Medical Society. They plan to revise our present Bylaws which have not been revised since 1908, and present them at a future meeting.

V. Some discussion, again, on Malpractice insurance and its affect on various members of the Medical Society.

VI. Discussion of the affect of the loss of two new doctors in the Jonesport area.

KARL V. LARSON, M.D., *Secretary*

Kennebec

A meeting of the Kennebec County Medical Association was held at the Silent Woman in Waterville, Maine on March 20, 1975, with 43 members attending. The meeting was called to order by the President, Dr. Joseph J. Hiebel.

The minutes of the February meeting were dispensed with.

Two new members were accepted into the organization, Drs. Albert Pepe of Waterville and Helen Mitchell of Augusta. The application of Dr. Walter Schuyler was read.

Dr. Teodoro C. Dela Cruz of Augusta presented a paper which had been drawn up by the Association of Neurological Surgeons regarding the current malpractice insurance. His paper outlined several reasons for the development of the crisis both from the standpoint of the medical profession and the insurance field, and also outlined several possible solutions to the crisis. Dr. Hiebel

commented that Dr. Dan Hanley of the Maine Medical Association had been invited to speak to the Association at the April meeting concerning this. Dr. Green of Waterville raised the related, but separate issue of the catastrophic illness program and the cost of catastrophic illness and made a motion that the Association report the appropriation of funds for the implementation of the act. A letter will be prepared by the Secretary and sent to the Legislative Appropriation Committee and to the Governor.

Dr. Hiebel then introduced Mr. Richard Nellson of the Associated Hospital Service of Maine who described to the members of the Association the present status of 80% UCR insurance. He indicated that only a relatively small portion of insured population are currently covered by these plans. It was apparent that there was considerable confusion on the part of the membership of the Association relating to the difference of the various Blue Cross plans, Medicare and Medicaid plans. It was further evident that the members of the Association did not feel that they were getting adequate feedback from the Insurance Committee of the Maine Medical Association. Many physicians also felt that they were not getting adequate information from the Associated Hospital Service. However, other physicians pointed out that many physicians did not bother to attend the County meeting and were not aware of the Blue Cross page in the State Medical Journal and that it was the responsibility of individual physicians to keep themselves informed of developments in the insurance field. Mr. Nellson then discussed the probability of National Health Insurance Plan being developed in the near future and what this might mean for the medical profession. All in all, the discussion was most lively, enlightening, and I think helpful to both Mr. Nellson and the membership, and his attendance was certainly highly appreciated.

O. THOMAS FEAGIN, M.D., *Secretary*

Lincoln-Sagadahoc

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset, Maine on February 18, 1975. There were twenty-six members and guests present when the meeting was called to order at 8:38 p.m. by the Vice-President, Dr. David S. Hill.

The minutes of the January meeting were accepted as read by the Secretary-Treasurer.

A letter was cited from the Cumberland County Medical Society approving transfer in October 1974 of Dr. Aldo F. Liorente from that society to this.

The Board of Censors recommended that Dr. Geoffrey A. Stroud of Brunswick be accepted in transfer from Cumberland County as approved by the latter county society; the recommendation was unanimously approved.

Dr. Paul H. Dumdey then introduced Currier McEwen, M.D., who spoke on Ankylosing Spondylitis.

There was no old business.

Dr. Richard C. Leck then suggested that county society members consider an increase in State society dues in the near future; no definite amount was suggested. He spoke of Legislative Documents 448, 453, 406, 452, and 1208, which would alter laboratory licensing laws; Dr. Blackburn passionately supplied details.

There was a general but short discussion of malpractice insurance premiums. The meeting was adjourned at 10:00 p.m.

The regular monthly meeting of the Society was held on March 18, 1975 at The Ledges Inn, Wiscasset, with thirty-three members and guests present.

The meeting was called to order at 8:41 p.m. by the President, Dr. Ralph C. Powell. The minutes of the February meeting were read by the Secretary and accepted as read.

Dr. Powell introduced Dr. John B. Madigan, President of the M.M.A., who spoke on the afternoon hearing this same date in Augusta concerning the proposed medical school in Maine. He spoke also about threatened changes in the present way of medical life which are being proposed nationally. He stressed the need for concerted and effective political action by organized medicine and mentioned the fact that some medical groups must act as bargaining units with government and third-party payors. He pleaded for direction and enthusiasm from the membership; several questions by members were discussed. The suggestion was made by several that the members of this Society are ready to follow vigorous Association leadership.

In the absence of correspondence, committee reports, old and new business, Dr. Robert H. Dixon of the scientific program committee introduced Dr. P. Richard Cote of Bath, who spoke on fetal monitoring and showed a motion picture.

The meeting was adjourned at 10:00 p.m.

GEORGE W. BOSTWICK, M.D., *Secretary*

News, Notes and Announcements

American Association for Clinical Immunology and Allergy

The 1975 meeting will be held at the Riviera Hotel, Palm Springs, California, October 15-19, 1975.

Please direct inquiries to our Staff Administrator, Howard Silber, AACIA, P.O. Box 912, DTS, Omaha, Nebraska (402) 558-5345.

Annual Otolaryngologic Assembly November 8 through November 14, 1975

The Annual Otolaryngologic Assembly of 1975 will be held November 8 through November 14, 1975, in the Eye and Ear Infirmary of the University of Illinois Hospital. The Department of Otolaryngology of the Abraham Lincoln School of Medicine,

University of Illinois at the Medical Center, offers a condensed basic and clinical program for practicing otolaryngologists under the direction of Emanuel M. Skolnik, M.D., with Burton J. Soboroff, M.D., as co-chairman. This program is designed to bring to specialists current information in medical and surgical otorhinolaryngology.

Interested otolaryngologists should direct their inquiries to the mailing address: Otolaryngology, P.O. Box 6998, Chicago, Ill. 60680.

A separate, but correlated course, "Conference on Radiology in Otolaryngology and Ophthalmology" will be held this year on Friday and Saturday, November 28 and 29, under the guidance of Galdino E. Valvassori, M.D. For further information about the radiology conference, write to Professor Valvassori, Radiology Department, Abraham Lincoln School of Medicine, P.O. Box 6998, Chicago, Ill. 60680.

A TRIBUTE TO DR. RALPH A. GOODWIN, SR.

Dr. Ralph A. Goodwin, Sr., practicing in Auburn, Maine for nearly sixty years, was born in the eastern Maine town of Danforth on December 13, 1884, the eldest son of Herbert and Ella Mae Powell Goodwin. He attended elementary and secondary schools in Lincoln and graduated from Mattanawcook Academy in 1904. He and his brother Harold attended Bates College and were graduated from Harvard Medical School in 1913. Prior to settling in Auburn in 1916, Ralph served an internship at Rhode Island General Hospital, Providence, Rhode Island and following this, he spent a year in specialty training at the Providence Lying-In Hospital. On returning to Auburn, he married Helen Pulsifer and began his extensive medical and surgical practice. In 1920, he became a member of the surgical staff at the Central Maine General Hospital and was a member of the active and consulting staff until March 1975 when he was made an honorary surgeon. From the early 1920's until 1947, he was physician to Bates College, serving well many generations of Bates undergraduates.

On the occasion of his 80th birthday in 1964, he was presented a plaque by the Medical Staff of the Central Maine General Hospital, "In Tribute to his Many Years of Fine Service to the Community."

In 1920, in association with Dr. H. R. Farris of Oxford and Dr. W. I. Haskell of Lewiston, he purchased the famous Oxford Spring House in Oxford, Maine and operated it as a sanatorium for World War I veterans until it was destroyed by fire on April 6, 1924.

Dr. Goodwin is a member and past president of the Androscoggin County Medical Association and a member, past counselor and past president (1949-50) of the Maine Medical Association. Among honors bestowed upon him are fellowships in the American College of Surgeons and the American Medical Association.

Realizing the need for keeping abreast of the rapidly changing

field of medicine, Dr. Goodwin has been a consistent supporter of postgraduate education and, until recently, faithfully attended many educational programs offered in the area and elsewhere.

As a charter member of the Lewiston-Auburn Kiwanis Club and as its president in 1926, and also a member of the College Club of Bates College, a service club of Bates graduates, Dr. Goodwin has been an active participant in local activities both here and at Orr's Island where he has a summer home. Needless to say, boating and fishing are his prime leisure activities and his enthusiasm for the Maine Coast has been shared with the many friends and colleagues who have been his guests at the island.

Both Dr. and Mrs. Goodwin joined the High Street Congregational Church and were regular attendants at its services and participated in its parish activities as long as health permitted.

Dr. Goodwin was first and foremost a family doctor and many of his patients were treated by him from birth to death. It was only with great reluctance and a real sense of loss that he retired from active practice in January 1975 because of declining health. A former patient and friend from Framingham, Massachusetts spoke for countless former patients when he referred to Dr. Goodwin as a "keen diagnostician, skilled pilot of the Maine coast, ardent fisherman, generous photographer of the local scene, heart-warming companion and friend."

Whereas: Dr. Ralph A. Goodwin, Sr. has served his community, his friends and the Central Maine General Hospital so well over these many years;

Therefore be it resolved: that this testimonial be incorporated in the records of the Medical Staff of the Central Maine General Hospital in this his ninety-first year, as a tribute to this service, and that copies be forwarded to Dr. Goodwin, members of his family and to the Maine Medical Association for publication in its Journal.

The Committee on Resolutions
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Pelvic Lipomatosis

MEYER EMANUEL, M.D.* and WILLIAM H. ROBINSON, M.D.**

Many physicians have encountered and puzzled over the disorder known as Pelvic Lipomatosis which Engles¹ first identified as a distinct entity in 1959 with the reporting of five cases. In 1968, Fogg and Smyth² defined it more or less as "an overgrowth of fatty tissues limited to the perirectal and perivesical spaces in the pelvis." By 1974, one author noted that about 40 cases had been reported.³ When we recently admitted a patient whose clinical picture fitted the criteria of this syndrome, we were surprised to discover that the great majority of physicians to whom we mentioned pelvic lipomatosis had never heard of it before. It appeared justifiable to call attention again to this bizarre disease which is thought to be more common than is reflected in the literature.

CASE REPORT

L. P., a 33-year-old white male veteran, was admitted to the Veterans Administration Center at Togus March 26, 1975 because of mild intermittent hematuria. He had recently lost 45 lbs. During one period in the service, he had similarly lost 35 lbs. but apparently regained it later. In 1962, at the age of 20 while in the service, he had an episode of right flank and back pains after some heavy lifting. A urinalysis showed microhematuria. An intravenous pyelogram showed normal upper tracts but the bladder was described as being in a "higher position than average." The possibility of a mass below the bladder was considered but after a negative rectal examination it was concluded that he had no obvious urinary tract disease. Six years later while serving in Germany he had an onset of nausea, left flank pain and mid-stream hematuria. There was no flank tenderness. The abdomen was moderately obese. A barium enema showed an exceedingly straightened rectosigmoid colon with some concentric narrowing for 25 cm. and the rectum was displaced anteriorly from the sacrum. An IVP at this time again showed a bladder displaced upward into a teardrop shape. A urine culture was positive for *E. coli*. Cystoscopy showed what was described as bullous edema.

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**Staff Radiologist, Veterans Administration Center, Togus, Maine 04330.



Fig. 1. Left posterior oblique at 15 minutes during excretion urography showing "tear-drop bladder" and radiolucent defect (arrow). Ureter slightly dilated but caliceal system is normal.

Sigmoidoscopy to 25 cm. revealed a normal mucosa and this was further confirmed by a mucosal biopsy.

On Oct. 2, 1968, an exploratory laparotomy was performed. There was excessive fat throughout the retroperitoneal area, in the small and large bowel mesentery, prevesically, and in the omentum. The dome of the bladder lay midway between the umbilicus and the pubis. The left colon was reflected medially. The presacral space was examined down to the coccyx and revealed a copious amount of fat. The latter surrounded the



Fig. 2. Post evacuation during barium enema showing marked compression and elongation of rectum.



Fig. 3. Barium enema film showing elongation of lateral filled rectum. Note anterior displacement from sacrum.

bladder and rectum but did not have a pathological appearance. A frozen section showed normal fat. This was later confirmed by the permanent section. Large amounts of fat were removed from around the bladder and both ureters were considered to be free of disease. In view of the extensive presence of fat around the bladder and colon, the retroperitoneum, intestinal mesenteries and omentum it was felt by the operators "... that any attempt to completely extirpate the fat in the sacrum and vesical area would have subjected the patient to a procedure of greater magnitude than was warranted." The patient made an uneventful recovery. A follow-up examination of May 12, 1969 again showed an elevated bladder on the IVP. Cystoscopy showed what was interpreted to be infiltration of the outlet with inflammatory polyps.

Upon the present admission to Togus, the veteran showed no acute distress. The urinalysis showed microscopic red cells. His blood pressure was normal. An IVP showed essentially the findings described previously (Fig. 1). The upper tracts showed no hydronephrosis but there was slight distal ureterectasia. A barium enema showed the typical medial deviation, straightening and constriction of the lower colon (Figs. 2 and 3). A G.I. series carried out because of the weight loss and a complaint of some epigastric discomfort at times was normal. Cystourethroscopy was surprisingly easy in this patient. There were bullous edema-like excrescences on the floor and around the neck of the bladder. The ureter orifices could not be seen but were identified by the forceful jets of I. V. indigocarmine. A transurethral resection of the proliferative tissue between the orifices as well as the neck of the bladder was carried out. The pathological report was cystitis cystica (Fig. 4). Delayed postoperative bleeding necessitated a brief period of control by transurethral coagulation of the bleeding points. Antibiotic therapy was administered. Though he had not previously specified any difficulty with voiding he now stated that he could start the urinary stream more readily. The urine remained grossly clear. The patient will be followed periodically.

DISCUSSION

The salient radiological findings are a urinary bladder compressed and lifted upward from its normal level in the pelvis and a rectosigmoid colon which is also compressed and straightened, both being surrounded by a radiolucent zone of the soft tissues now recognized as fat.¹² A further interesting feature is the association with this picture of an irregular proliferation of the mucosa along the floor and neck of the bladder and hiding the ureter orifices. Biopsies of this tissue to rule out cancer have shown the process to be a cystitis varying as cystica or glandularis or follicularis. Often the ureters show evidence of obstruction by these excrescences in addition to the compressive effect of the surrounding fat.

The shape of the bladder is described variously as looking like a banana, a gourd or a tear drop. The rectosigmoid colon is not only compressed to a narrow straight structure but it is also deviated to the right. The radiolucency of the soft tissues of the pelvis has aroused a suspicion of malignancy and apart from direct biopsies, studies with pelvic arteriography have been done to exclude it.^{4,12} The bladder shadow often shows filling defects (Fig. 1) at the base suspicious of bladder tumors but these are now known to be the masses of proliferative mucosa (Fig. 4). In the patient we have presented the ureter orifices were well hidden within the poly-



Fig. 4. Cystitis cystica of bladder. Photomicrograph shows cysts on the surface of the mucosa and Brunn's nests in the submucosa. This finding is a manifestation of chronic cystitis (proliferative cystitis).

poid mucosal folds and could be demonstrated to be patent at cystoscopy only by the forceful jets of I. V. indigocarmine. To date there has been no report of a transition of this proliferative type of cystitis to malignancy,⁵ although this has occurred very rarely with cystitis glandularis in patients without the picture of pelvic lipomatosis.⁶

Most patients with pelvic lipomatosis cannot be cystoscoped because of the elongation and distortion of the prostatic urethra.^{7,8,12} In our patient, we were fortunate in being able to do so easily. Despite this, many of the patients have no difficulty in voiding.⁸ Sigmoidoscopy is not remarkable except for the straightening of the lower colon. An unusual case reported by Schechter³ included obstruction of the vena cava.

Of the cases reported, more than half appear to be in blacks and so far there is only one report in a female.⁹ Prognosis is poorer in the younger patients who are typified as stocky or obese likely to have hypertension, hematuria, urinary symptoms and ureteral obstruction which may lead to uremia. In patients over 60, the outlook is less ominous.^{2,12} Many of the patients have no symptoms.¹² When present, they may include nausea, vomiting, mild low abdominal discomfort, constipation with narrow stools, hesitancy in voiding and hematuria.¹

When the abdomen is palpated, some patients present a vague suprapubic mass which fluctuates in prominence probably as the bladder is full or empty. Rectal palpation may disclose a highly positioned prostate gland.

The etiology is unknown. In one case report, a patient with the findings of pelvic lipomatosis also showed multiple fatty deposits elsewhere over the body compatible with Dercum's Disease (adiposis dolorosa).¹⁰ Gain or loss in weight does not seem to be associated with this disorder.^{5,9} When patients have been explored, the fat examined by various analytical methods proves to be entirely normal with no evidences of malignancy. There is associated vascularity, fibrosis, evidences of inflammation and hemorrhages.^{1,4,11,12}

While most reports express the impracticability of attempting removal of all the fat surgically,^{2,4,7,11} Carpenter⁵ carried out extensive dissection of the fat to free the ureters into the pelvis and to uncover the bladder. The operation took four hours and six units of blood. Other authors report attempts to at least free the ureters when urgently required to relieve obstruction. Other operative procedures have included transurethral resection of the proliferative cystitis process on the floor of the bladder, bladder neck and posterior urethra, ileal loop conduit, reimplantation of the ureters into the bladder, intraperitonealization of the ureters as in retroperitoneal fibrosis, cutaneous ureterostomy, nephrostomy, nephroureterectomy and cystostomy.

There is no definitive conservative therapy. Radiation has been of no benefit.^{4,12} Steroids having failed in retroperitoneal fibrosis and periureteritis and pericystitis plastica are considered an unlikely answer. The only practical recommendation is the use of long term antimicrobial therapy.⁴

SUMMARY

The case of a patient with pelvic lipomatosis is presented in the belief that many physicians are not familiar with this clinical entity which was first identified as recently as 1959 and which is thought to be more prevalent than is reflected in the literature. The disorder is characterized by massive overgrowth of normal fat tissue chiefly within the pelvis surrounding the bladder and lower colon compressing and lifting both into a distorted disposition while also compressing the lower ureters. Roentgenologically the fat is seen as a translucent zone about the pelvic viscera. Associated with this picture is the inflammatory proliferative process involving the mucosa of the floor, neck of the bladder and sometimes the posterior urethra which is pathologically described variously as cystitis cystica, glandularis or follicularis. This process along with the perivesical fat may result in upper tract obstructive changes

Continued on Page 193

Postoperative Shock Lung

Report of a Case and Discussion of its Relationship to Chronic Shock*

FENNELL P. TURNER, M.D.**

"Shock lung" with its many synonyms has been studied extensively during the past six or seven years. The diagnosis is sometimes made postoperatively in patients who have been severely ill. It also is found in patients who have experienced severe trauma. Reproduction of the exact syndrome in an experimental model, however, has met only with limited success, and the pathogenesis of the syndrome remains in doubt. For this reason, it is believed that a report of a case of shock lung will be of interest.

CASE REPORT

A 51-year-old man was admitted to the Togus VA Center on 8/4/70 by transfer from the VA Hospital in Cleveland, Ohio. He had been on a trans-continental automobile trip when, because of the sudden onset of chills, fever and malaise he was admitted to a community hospital on 6/25/70. He was found to have pneumonia in the right lower lobe and this was soon followed by involvement of the right middle lobe. Sometime later the left lower lobe became involved and, in addition, he showed evidence of pleural effusion.

He was transferred to the VA Hospital, Cleveland, Ohio on 7/8/70. Although for a period of time while in Cleveland there was shortness of breath, intermittent left chest pain, and occasional cough with hemoptysis, the diagnosis of thromboembolism was never established. Blood gas studies had shown a mild hypoxemia and respiratory alkalosis (Table 1). There was also moderate hypoproteinemia, icterus and elevation of serum enzymes (Table 2).

Bronchoscopy revealed hyperemia of the basilar bronchi consistent with bronchial inflammation and bronchial washings grew *Neisseria catarrhalis* and *Streptococcus viridans* under culture conditions. Throat and sputum cultures demonstrated normal flora and several blood cultures were negative. Smears and complement fixation tests for acid fast bacilli and fungi were negative. Plans were made for transfer to a hospital closer to home and it was suggested at the time of transfer that a lung biopsy be carried out because of the persistent density at the left base.

On admission to VAC Togus, Maine on 8/4/70, a review of his past history showed that he had worked for many years in a linoleum factory and that he had smoked one to three packs of cigarettes per day for about 30 years. On physical examination there was a low-grade fever, moderate pallor, and he appeared chronically ill. There was dullness to percussion over the lower left chest and diminished tactile fremitus. A few moist expiratory rales were heard in this area. Laboratory studies revealed the following values: hematocrit, 35%; hemoglobin, 10.9 gm/100cc.; sedimentation rate, 95 mm/hr.; reticulocytes, 3.2%; pulmonary function tests were at the lower limits of normal; ECG, normal; sputum samples obtained by super-heated steam showed atypical cells and repeated x-rays of the chest showed a persisting lesion at the left base (Fig. 1). The differential diagnosis was

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TABLE 1

ARTERIAL BLOOD GAS STUDIES				
	pH	PO ₂	PCO ₂	O ₂ Sat.
Normal Values	7.36-7.46	80-100	35-45	97
7/17/70 air	7.49	51	34	88
9/25/70 nasal O ₂ 5 l/min.	7.54	26	29	60.5
9/25/70 100% O ₂ mask	7.49	83.5	33	96.5
46% right to left shunt				
9/26/70 ventilator 10 l/min.	7.56	91	35.25	97.8
9/30/70 ventilator 10 l/min.	7.56	195	36.75	99.4
10/13/70 air	7.50	58	34	91.6

TABLE 2

SERUM PROTEINS AND ENZYMES						
	Total Proteins	Albumin	Bilirubin	Alk. Phos.	LDH	SGOT
Normal	6-8	3.5-5	0-1	30-85	90-200	20-50
July 9	5.9	2.1	2.8	265	475	250
July 10	5.9	2.2	1.3	235	250	130
July 14	6.2	2.2	.6	200	205	85
July 16	6.6	2.5	.6	165	145	60
July 21	6.9	2.8	.4	155	140	30
July 27	6.6	2.9	.4	125	145	25

believed to lie between organized interstitial pneumonitis, inflammatory pseudotumor or bronchogenic carcinoma. An exploratory thoracotomy was carried out on 9/21/70, approximately three months after onset of his present illness. At operation, he was found to have extensive pleuritis over the left lower pleural cavity with fixation of a firm egg-sized mass to the thickened parietal pleura at the costophrenic angle. There were a number of enlarged hilar lymph nodes, and a few emphysematous blebs from 3-4 cms. in diameter were found in the apex of the left upper lobe. Frozen sections of lung, pleura and nodes were all negative. While dissecting in the major fissure, it was found that the artery to the basilar segments of the left lower lobe was firmly thrombosed and, accordingly, a left lower lobe lobectomy was carried out. There was a moderate blood loss due to the pleural dissection and following a blood transfusion the postoperative condition was considered good.

The immediate postoperative course was satisfactory. He coughed easily, the lung rapidly expanded and air leakage had ceased by the second postoperative day. At this time, an x-ray examination showed slight elevation of the left diaphragm and some fluid at the left base. There was also a small amount of plate-like atelectasis at the right base. The lung, however, was clear to auscultation. Keflin® was given intravenously, and heparin was also given because of the operative evidence of arterial thrombosis and pulmonary infarction. On the third postoperative



Fig. 1. Preoperative roentgenogram of chest showing persistent elevation of left diaphragm associated with atelectasis and/or pneumonia, basilar segments left lower lobe.

day, there was a slight increase in dyspnea and a chest x-ray showed some haziness. By the fourth postoperative day, he was noticeably dyspneic, quite restless, slightly cyanotic and his neck veins were slightly distended. He coughed easily with a slightly yellowish sputum, and auscultation revealed fairly normal, perhaps diminished, breath sounds. There were no rales. An x-ray of the chest showed a postoperative chest with expansion of the LUL and some fluid at the left base together with bilateral diffuse fluffy infiltrates and a generalized hypolucency (Fig. 2). Blood gas studies while on nasal oxygen of 5 liters per minute showed a pH of 7.54, PO_2 of 26, PCO_2 of 29 and O_2 saturation was 60.5 (Table 1); 100% oxygen was then given by mask and a 46 percent right to left shunt was found. Accordingly, a tracheostomy was carried out and the patient was placed on an Emerson volume controlled ventilator. Heparin was continued, furosemide was administered and (because of the distended neck veins) digitalization was carried out. A culture of sputum taken the day before showed only *Streptococcus viridans* and *Neisseria catarrhalis* and at the time of tracheostomy it was observed that tracheal exudate was minimal. A Gram stain of a smear of this secretion showed a mixed flora with a few negative organisms. Despite this report, and for fear that the patient also had a cephalothin-resistant Gram negative interstitial pneumonitis, gentamycin was added to the treatment schedule. The report of tracheal culture, however, demonstrated only "normal flora." Three days later, on 9/28/70, another culture was obtained from the tracheostomy and this showed a heavy growth of *Aerobacter aerogenes* together with *S. viridans* and *N. catarrhalis*. It is believed that this organism represented a secondary opportunistic invader as did a culture of *Pseudomonas aeruginosa* obtained two weeks later. Plasma electrolytes obtained prior to tracheostomy were as follows: sodium, 144 mEq/L; potassium, 6.1; chloride, 104; and carbon dioxide, 20. On subsequent days, the potassium fell to 4.8 and then 3.5. There was striking clinical

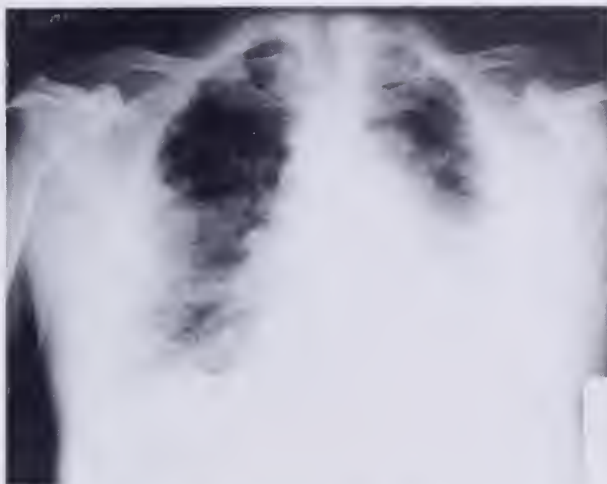


Fig. 2. Chest film taken on fourth postoperative day demonstrating diffusely disseminated interstitial and/or alveolar densities in both lung fields characteristic of "shock lung."



Fig. 3. Chest film on fifth postoperative day showing persistence of the diffusely scattered fluffy areas of infiltration.

improvement within a short time of being placed on the ventilator characterized by slowing of pulse, change in color, and improvement in arterial blood gas values. The radiographic findings, however, persisted for several days (Fig. 3) and the temperature subsided slowly by lysis. He remained on the ventilator for six days and was gradually weaned from the machine for the last two days of this time.

In the meantime, pathological examination of the surgical specimen confirmed the operative findings of arterial thrombosis and pulmonary infarction of basilar segments LLL. The tissue removed also showed coagulation necrosis within the area of infarction and an extensive acute and chronic inflammatory reaction around the area of infarction. There was marked fibrosis and numerous macrophages. A number of microscopic abscesses were seen in the lung. In addition, surrounding the area of infarction, there were numerous carbon particles, asbestos bodies and multi-nucleated giant cells. Finally, retrospective review of the hematocrit and hemoglobin levels (Table 3) showed evidence of preoperative anemia, an immediate postoperative hemoconcentration and this was followed by low hemoglobin and hematocrit values which persisted for more than three weeks. Preoperative hypovolemia and anemia followed by an inadequately replaced

operative and immediate postoperative blood loss estimated to be from 1000 to 1250 ml. would explain these laboratory findings.

DISCUSSION

We have presented the case of a patient who had a left lower lobe lobectomy for an undiagnosed lung lesion of three months' duration. He may have originally had a true right lower lobe pneumonia,

TABLE 3

HEMATOCRIT AND HEMOGLOBIN; RESPONSE TO SURGERY		
	Hematocrit	Hemoglobin
Pre-op	35 → 37	10.9 → 13.2
9/21/70	Operation — 1 Transfusion	
Post-op day 0 → 6	35.5 → 30	10.0 → 8.1
9/28/70	1 Transfusion	
Post-op day 7 → 22	31 → 36	8.6 → 11.2

TABLE 4

SYNONYMS FOR "SHOCK LUNG"
Adult respiratory distress syndrome
Postoperative respiratory distress syndrome
Postoperative (post-traumatic) pulmonary insufficiency
Postoperative (post-traumatic) wet lung
Diffuse atelectasis
Non-obstructive atelectasis
Congestive atelectasis

but repeated episodes of hemoptysis and the later development of a persistent lesion in the left lung would indicate that pulmonary infarction was a major reason for his prolonged hospitalization. Although no evidence of peripheral thrombophlebitis was ever observed, the elevated serum bilirubin, alkaline phosphatase and LDH were all consistent with his diagnosis. It is even quite probable that thrombo-embolic disease was the real reason that forced him to discontinue his automobile trip from California to Maine. After a prolonged hospitalization of more than three months in three different hospitals, this chronically ill, middle-aged man was subjected to exploratory thoracotomy and resection of the left lower lobe. Despite a satisfactory immediate postoperative course, several days later he developed characteristic symptoms which have

TABLE 5

LUNG SYNDROME WITH PATHOPHYSIOLOGICAL CHANGES SIMILAR TO THOSE OF SHOCK LUNG
Post-perfusion (post-pump) stiff-lung syndrome
Post-perfusion (post-pump) capillary-leak syndrome
Pulmonary edema of cardiac failure
Diffuse interstitial pneumonitis
(Usually Gram-negative organisms)
Aspiration pneumonitis
Post-burn lung or smoke inhalation

TABLE 6

THE VICIOUS CIRCLE (V. H. Moon — 1940)

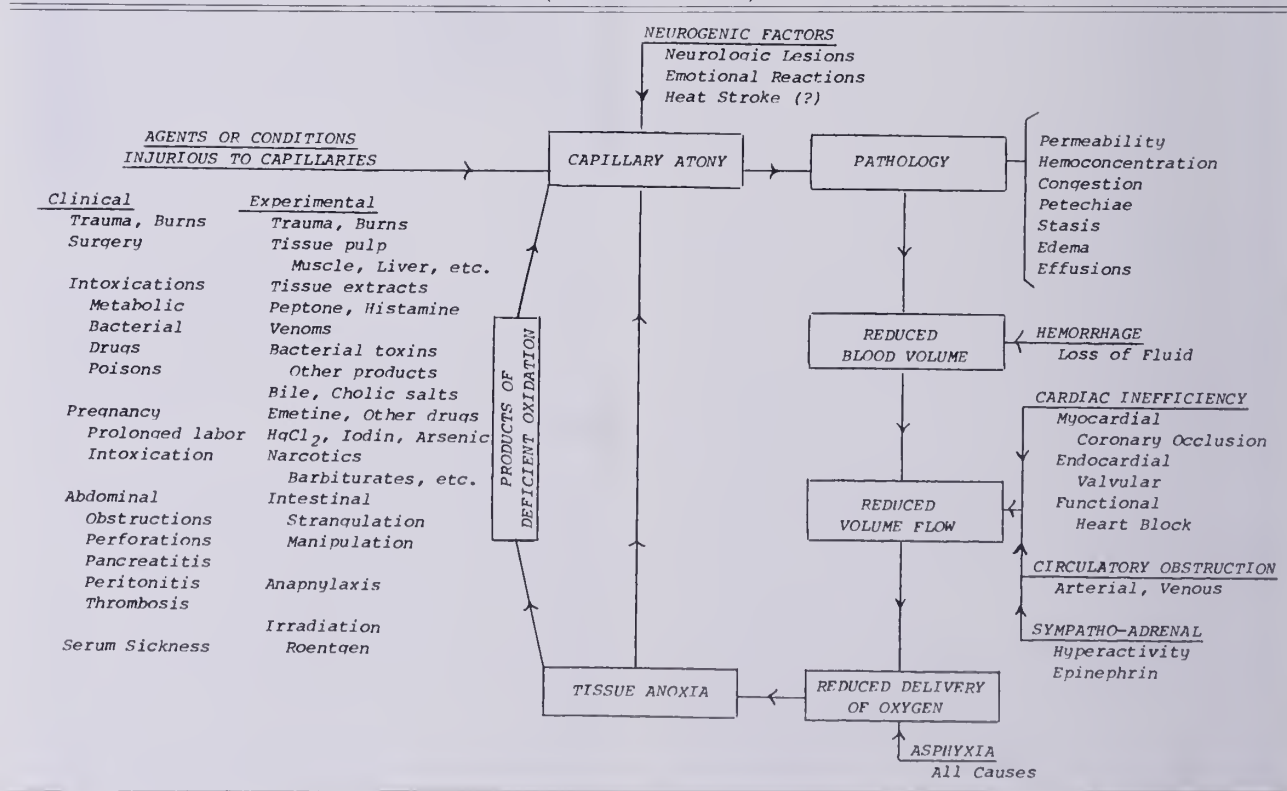
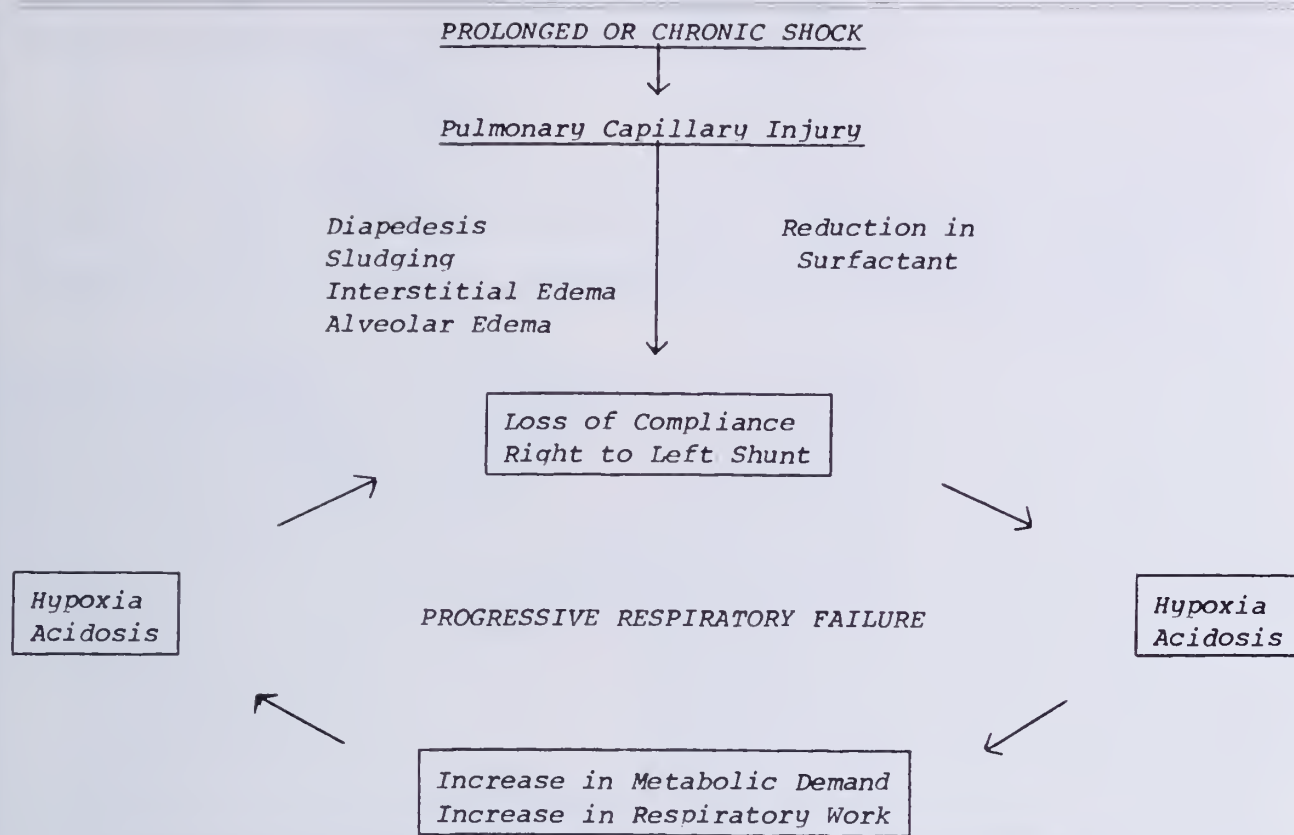


TABLE 7



been called by many names including: adult respiratory distress syndrome, congestive atelectasis and shock lung (Table 4).

This is a syndrome about which much has been written during the past six or seven years. It was observed and thoroughly studied during the Viet Nam Conflict and the diagnosis and management has now become somewhat standardized. The contributions of many authors on this subject have recently been summarized in a recent issue of the *Surgical Clinics of North America*.¹ Certain puzzling features remain, however, and although the pathological findings observed by study of pulmonary tissue are well recognized, the pathogenesis of the defect remains in doubt. I believe it would be correct to say that there are many pulmonary changes due to diseases widely different in etiology that can be confused with the picture of shock lung, simply because pulmonary tissue has a limited way of responding to injury. Cardiac decompensation, diffuse interstitial pneumonitis, endotoxic and chemical injuries to the bronchioles and alveoli such as observed in septic shock, aspiration pneumonitis, and heat or smoke inhalation all can produce changes similar to those found in shock lung (Table 5). The post-perfusion capillary leak syndrome is also said to show certain histological similarities. However,

it is pulmonary failure of the type seen in a person who also has evidence of secondary (hypovolemic) shock with which we are presently concerned. Here, I believe, shock itself is of etiological significance. With acute shock of relatively short duration shock lung does not develop and this is why it has been impossible thus far to find shock lung following acute hemorrhage in the experimental animal. Instead, it is in chronic shock² where the state of shock has been sufficiently prolonged or protracted (as by definition, chronic means long continued) that the characteristic pulmonary lesion will develop. Pathological findings of this nature were observed thirty and forty years ago at the post-mortem table and were attributed to the "duration of the shock state as patients dying early in shock did not show it."² Chronically ill and debilitated patients were found to be particularly prone to respiratory failure and Moon³ has called this a state of "sub-lethal" shock. Turner² found this term inaccurate as many such patients did die and came to autopsy examination and he first used the term "chronic shock." Five years later, Clark and Lyons⁴ also were to use the term chronic shock in describing these malnourished and depleted patients.

For more than one hundred years instances of primary shock have been recognized. Goltz⁵ in 1863

had found that a blow to the exposed mesentery of a frog caused a reflex inhibition of the heart through the vagus and a lessening of vascular tone in the splanchnic area. Similar primary shock of neurogenic origin will result from a head injury. However, it was not until World War I and the succeeding years that the true nature of secondary or hypovolemic shock became understood through the work of Cannon, Bayliss, Blalock, Parsons, Phemister and others. Blood and plasma loss, and loss of extra-cellular fluid and electrolytes were all recognized as events resulting in the loss of an effective circulating blood volume. The decrease in the oxygen carrying capacity of blood and the reduction in colloid osmotic pressure further aggravate the hypovolemia and subsequent secondary vaso-constriction of the hemorrhagic, burned or dehydrated patient by further decreasing tissue perfusion and increasing capillary damage. Cellular hypoxia, capillary stasis, dilatation and increased permeability, anaerobic metabolism and acidosis now take place which adds even further to the inadequacy of tissue perfusion. Moon called this "circulatory failure of capillary origin" and his well known "Vicious Circle" of Shock (Table 6) gathers together most of the agents and events which cause capillary injury and result in impaired tissue perfusion. Others have since called this the "shock wheel."

The effect of circulatory failure of capillary origin on pulmonary tissue is striking. Capillary stasis and dilatation, sludging of blood cells, increased capillary permeability, leakage of fluid, diapedesis of blood cells, perivascular hemorrhage and interstitial and alveolar edema are the characteristic histological findings. The gross appearances are similarly striking and the pathophysiological cause, as well as effect, of this congested, edematous and heavy lung is of course anoxia (Table 7).

Slowing of blood flow and swelling and edema of interstitial tissue, as well as of the alveolus itself, results in a decrease in the rate of diffusion of gases (oxygen and carbon dioxide) across the capillary alveolar membrane. There is arterio-venous admixture of blood gases within the pulmonary circulation and the poorly oxygenated blood is similar to that found in a patient with congenital heart disease where there is right to left shunting of blood due to a congenital defect such as a patent foramen ovale. Loss of compliance due to the increasing inability of the patient to expand his congested lung is the other characteristic finding.

Oxygen administration has long been a cornerstone of therapy for patients in cardiac failure and in patients with severe lobar pneumonia where long ago it was recognized that the effect of pulmonary shunting together with the diminution of vital capacity in such patients resulted in severe hypoxia. Oxy-

Continued on Page 185



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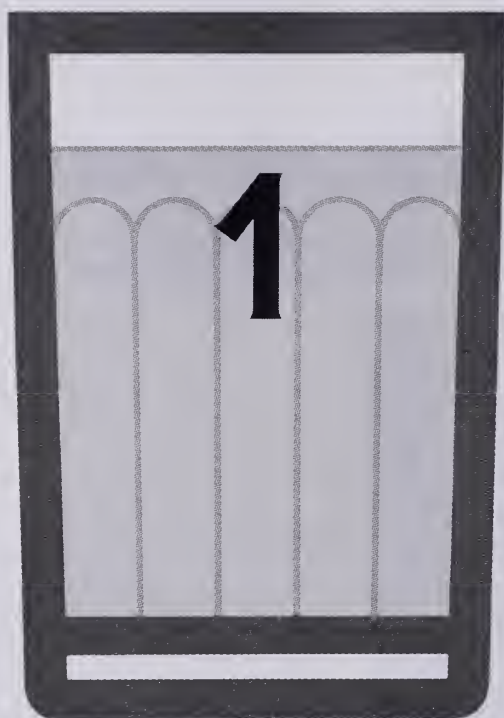
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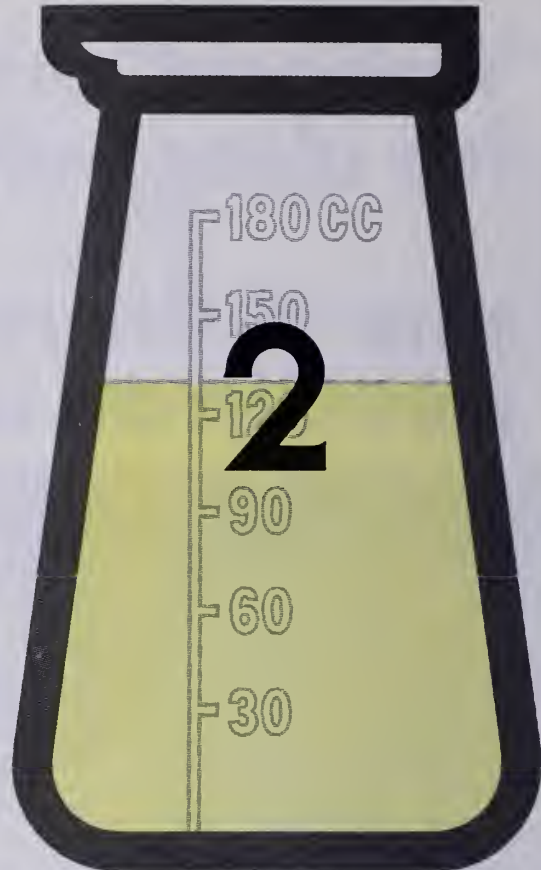
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Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

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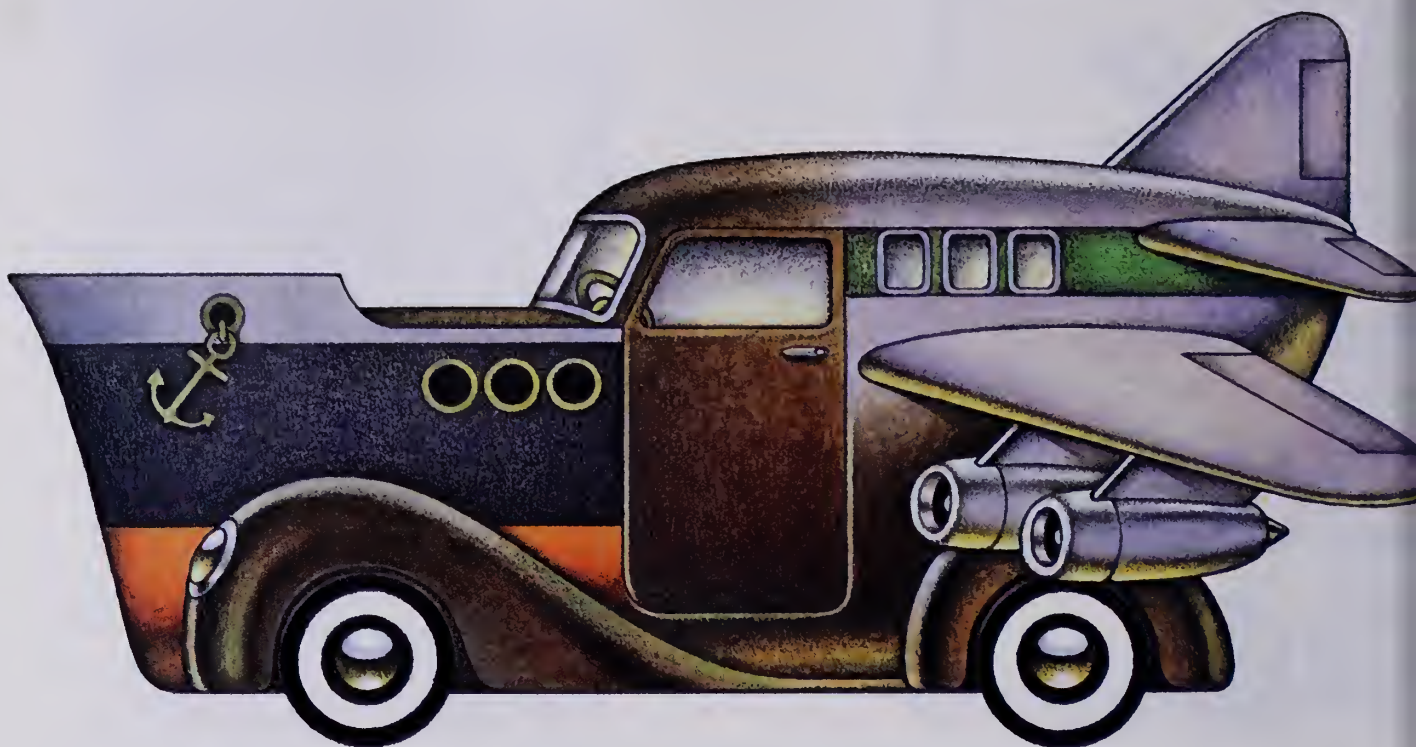
Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs b.i.d. Maximum dose should not exceed 75 mg/kg/24 hrs.

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TABLE 8

DIAGNOSIS OF SHOCK LUNG

1. Few reliable early changes in ventilatory function to indicate onset of shock lung
2. Patient looks good for 24-48 hours after operation or stressful event
3. Gradual onset of tachypnea, dyspnea, tachycardia, fever and cyanosis
4. Striking absence of moist rales
5. X-ray of chest shows extensive scattered fluffy areas of infiltrate, sometimes a ground glass appearance with generalized hypolucency
6. Arterial blood gas studies show hypoxemia and hypocarbia
7. Hypercapnia, a late sign of respiratory failure

TABLE 9

TREATMENT OF SHOCK LUNG

1. Volume cycled ventilator if arterial PO_2 less than 60
2. Positive end expiratory pressure (PEEP) at 5-10 cms. H_2O
3. Tracheostomy sometimes required
4. Correct hypovolemia
 - a. Replace blood loss with blood
 - b. Give serum albumin for hypoproteinemia and to reduce interstitial pulmonary edema
 - c. Isotonic electrolyte solution in extracellular dehydration
 - d. Give saline sparingly
 - e. Dextran to improve microcirculatory blood flow
5. Diuretics (furosemide) to mobilize excess fluid
6. Digitalis if suspected failure
7. Antibiotics for infection
8. Heparin if thromboembolism suspected and also in presence of disseminated intravascular coagulation
9. Adrenal steroids for correction of capillary permeability and for stabilization of lysosomal membranes

gen administration under increased pressure to patients who had experienced severe trauma had also been carried out occasionally with success, particularly by anesthesiologists. However, the need for long-term mechanical ventilation in the conscious patient had not been widely recognized until recent years, nor was the instrumentation for this therapy available.

The early diagnosis of shock lung is difficult (Table 8). It is of value to have a high index of suspicion, and it is of even greater value to order sufficiently frequent blood gas studies so as to keep in touch with the changing pulmonary picture. Whereas, the signs and symptoms of anoxemia usually appear when the oxygen saturation is around 85%, which would be what we would expect with a PO_2 of less than 60, many elderly patients with chronic obstructive lung disease are slightly hypoxic and that would be about the lower limits of normal in this group. Sleeplessness, delirium, cyanosis and dyspnea generally start to appear with values below this level and in patients with an arterial O_2 saturation of less than 80% and PO_2 of about 40-45 the mortality will be quite high without strenuous therapy. It should be re-emphasized at this point that the postoperative patient, particularly after chest sur-

TABLE 10

PREOPERATIVE PATIENT EVALUATION
(Conditions to treat and/or recognize)

Chronic obstructive lung disease
(emphysema and bronchitis)
Restrictive lung disease
(fibrosis and pleuritis)
Cardiovascular disease
Thrombo-embolic disease
Preoperative trauma
Anemia — hypovolemia
Weakness — debility
Malnutrition — hypoproteinemia
Immobilization — bed — chair
Acute and chronic infection
Obesity — ascites — peritonitis
Hepatic and renal disease

TABLE 11

PREOPERATIVE MEASURES FOR THE
PREVENTION OF POSTOPERATIVE SHOCK LUNG

1. Correct, or make note of, deficiencies found on preoperative patient evaluation
2. Preoperative pulmonary physiotherapy
 - Breathing and coughing exercises
 - No smoking
 - Intermittent positive pressure breathing
3. Preoperative psychotherapy — establish rapport with patient
4. Allay fears and anxiety

TABLE 12

POSTOPERATIVE MEASURES FOR THE
PREVENTION OF POSTOPERATIVE SHOCK LUNG

1. Adequate blood and fluid replacement
2. Active postoperative pulmonary physiotherapy
 - Deep breathing exercises
 - Blow bottle — rebreathing devices
 - "Incentive spirometry"
 - Mucolytic agents and bronchodilators if required
 - Coughing with pressure
3. Frequent change of position — turn from side to side every 1-2 hours
4. Relief of pain and anxiety
5. (?) Prophylactic use of serum albumin in large amounts to mobilize interstitial fluid and prevent development of suspected early shock lung

gery, will often look deceptively good for one to two days.

The treatment of shock lung is now fairly well systematized and the mainstay of treatment is the volume cycled ventilator (Table 9). By mechanical ventilation of the patient, arterial oxygen saturation is increased, the requirement for increased cardiac output is diminished, physical work of respiration is diminished and atelectatic alveoli are re-expanded. The provision of adequate amounts of oxygen breaks the cycle of anoxia, capillary damage, slowing of blood flow and further anoxia. In addition, it should be remembered that continuous positive pressure ventilation has resulted sometimes in the successful resuscitation of a patient in pulmonary

failure who was not responding to intermittent positive pressure ventilation. It is believed that this may have some relationship to the available supply of surfactant. Damage to alveolar type II cells by anoxia and diminished surfactant may possibly have some part to play in the development of additional pulmonary shunting and venous arterial admixture. Other mainstays in the therapy of shock lung are replacement of whole blood, maintenance of serum protein level, administration of diuretics to mobilize excessive interstitial and intra-alveolar water and digitalization of the patient if there is any question of cardiac failure.

The routine use of heparin, dextran, and methylprednisolone is more controversial. Both heparin and dextran have been recommended in order to reduce red cell and platelet aggregation and as a way to improve microcapillary blood flow. Adrenal steroids in pharmacological doses have been recommended. The objective here is to decrease capillary permeability and to stabilize lysosomal membranes thereby preventing the release of hydrolytic enzymes into the circulation as well as into the surrounding tissue. Adrenal steroids are believed to have a large number of other beneficial effects in the treatment of shock. However, the experimental evidence supporting much of this remains controversial. Neither dextran nor methylprednisolone were administered in the patient's case just presented.

Finally, the best treatment is prevention. In a case like the one just presented, a more perceptive preoperative patient evaluation might have brought us to understand the nature of the operative risk with which this patient was being confronted (Table 10). Recognition of these additional factors would result also in the institution of certain preoperative and postoperative measures aimed at the maximum preparation of the patient for surgery (Tables 11 and 12).

SUMMARY

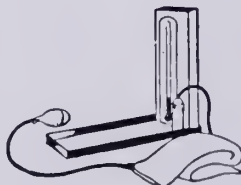
This 51-year-old man had had an illness of about three months' duration which consisted of pneumonia in the right lung followed by thromboembolism, bilateral, and characterized by prolonged hos-

pitalization, fever, hypoproteinemia, and anemia. Despite acceptable pulmonary function studies, this patient was found later to have pre-existing asbestosis, pulmonary fibrosis and chronic obstructive lung disease with bullous emphysema. Because of this prolonged and debilitating illness and in view of the anemia and hypoproteinemia, we can assume also that there was a diminished blood volume at the time of surgery.

Although the operation was carried out without basic difficulty, some extra-pleural dissection was required in view of the dense adhesions at the left costophrenic angle and the blood loss was estimated to be from 1000 to 1250 ml. In view of the later evidence of some fluid at the left base, the blood loss might have been greater. He received 500 cc. of blood during surgery which in retrospect most probably was inadequate. The slight hemoconcentration (in view of subsequent hematocrit values) during the first two postoperative days would tend to agree with the retrospective diagnosis of inadequate blood replacement and this, together with the likelihood of a diminished blood volume prior to operation, would lead to the development of moderate hypovolemic shock and reduced capillary perfusion of vital organs. This hypovolemia, added to a pre-existing C.O.L.D. and asbestosis, was sufficient in this post-thoracotomy patient to result in the severe hypoxia characteristic of the acute respiratory distress syndrome.

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Hyaline Membrane Disease of the Newborn, Revisited

PETER B. MACOMBER, M.D.*

ABSTRACT

The exact mechanism by which hyaline membranes are formed and their significance in the pathogenesis of hyaline membrane disease of the newborn is not clear. The membranes are composed of degenerating alveolar epithelium admixed with plasma derived substances including fibrin. They require a period of air breathing for their formation. Components of pulmonary surfactant are scavenged by the membranes. Several plasma components inhibit surfactant activity. Recovery from the disease does not occur until new epithelium regenerates and undergoes functional maturation. It is postulated that functional surfactant deficiency at birth causes failure of the majority of alveoli to become aerated which causes overdistention of the alveolar ducts especially during inspiratory efforts. These stretching forces tear epithelium from the basement membrane resulting in rapid enzymatic cell degradation with subsequent defects of the basement membrane which permit entrance of plasma elements which combine with the degenerating epithelium. Since the disease may be reversible before epithelial injury has occurred, it is recommended that trials be conducted using experimental models of hyaline membrane disease to determine whether intratracheal administration of pulmonary surfactant of natural origin at the moment of birth might prevent the development of the disease.

During my training as a resident in pathology in 1954 to 1958, I became familiar with a mysterious disease involving newborn infants. This disease was the cause of death in 5% of all autopsies I performed during the residency and 38% of autopsies on infants dying in the first week of life. Because so little was known about the etiology and treatment of the disease and it was so common, it became a subject of great interest and frequent speculation among my fellow residents in pediatrics and pathology.

This disease is now known either as hyaline membrane disease of the newborn or idiopathic respiratory distress syndrome of the newborn. Its clinical and pathologic features have been well described.^{1,2,3,4} The disease develops chiefly in premature infants and is more likely to occur if there has been an episode of intrapartum fetal anoxia. The incidence is likewise increased in the presence

of maternal diabetes, the second born of twins, in families with a prior history of hyaline membrane disease, and at least in some cases after Caesarean section.⁵ In cases involving maternal bleeding, the incidence of hyaline membrane disease is reduced if the mother is brought out of shock by blood transfusion prior to performance of a Caesarean section.¹ The disease is characterized by the development of dyspnea, cyanosis, sternal retractions, and grunting respirations, either at the time of birth or within the next few hours. If death occurs from the disease itself, it is almost always within the first three to four days after birth. At autopsy the lungs are congested, meaty in consistency, and nearly airless. Microscopically, there is widespread atelectasis of the majority of the alveoli while scattered alveolar ducts are hyperdistended by air and others are lined by hyaline membranes. If one attempts to reinflate the lungs with air, the lungs of babies dying of hyaline membrane disease are found to be much less distensible than the lungs from newborn babies dying of other causes.

In the year following my residency training, I encountered a case of hyaline membrane disease in a 570 gram infant who died 5 hours after birth. Hyaline membranes were beginning to develop in what could be clearly identified as partially sheared off alveolar duct epithelium. This baby had a twin of similar weight who died 20 minutes after birth. Since both babies were moribund at the time of birth and the longer survival of one seemed almost a chance event, I reasoned that an examination of the lung of the twin dying first might give a view of an earlier stage of the disease. The chief finding was one of generalized severe atelectasis with extreme overdistention of isolated alveolar ducts many of which showed beginning desquamation of the lining epithelium. This suggested that shearing forces resulting from overdistention of alveolar ducts might tear the epithelium off the basement membrane causing it to degenerate and form the nidus of a hyaline membrane.

Until the present I have not had an opportunity to pursue the subject. However, when Dr. Cuprak invited members of the staff at Togus to present papers on the subject of respiration at this symposium, I thought this might be a good chance to renew my acquaintance with hyaline membrane disease and find out whether my hypothesis was of any value in reaching an understanding of the patho-

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genesis of the disease. Reviewing this subject after so many years has given me a feeling similar to what Rip Van Winkle must have felt when he awoke after sleeping for twenty years. The number of excellent studies which have been carried out on this subject in the past twenty years is truly phenomenal. Many old ideas have been discarded and many phenomena of the disease have been satisfactorily explained, but the overall pathogenesis is still unclear. Many hypotheses have been advanced only to be discarded as more information has been accumulated. Realizing this has made me humble about my own speculations and I hope my ensuing remarks will be accepted in this vein.

Of the many factors which have been proposed to play a role in this disease, three stand out and seem especially worthy of discussion. These are pulmonary surfactant deficiency, constriction of the pulmonary arterioles with hypoperfusion of the lungs, and necrosis of alveolar epithelium with hyaline membrane formation. Of the three, pulmonary surfactant deficiency has probably been most thoroughly investigated.^{2,3}

Pulmonary surfactant is secreted in the alveoli of the lungs. It has the special property of lowering surface tension as the surface which it covers is reduced in area. This keeps alveoli which have expanded from collapsing during expiration. This property is imparted chiefly by surface active phospholipids such as lecithin. In addition to this surface layer, there is a thin liquid hypophase layer separating the surface of the alveolar epithelium from air in which are found mucopolysaccharides, sialomucins, micelles of phospholipids, and possibly also enzymes that convert precursor molecules into active phospholipids. Several plasma components are known to be capable of inactivating surfactant. These include fibrinogen, a phospholipase, and probably also a third as yet unidentified substance.^{6,7}

The fetal lung secretes a fluid which is rich in pulmonary surfactant and low in specific gravity. This fluid is generally rapidly resorbed after air breathing commences. Amniotic fluid is of higher specific gravity and lacks significant surfactant activity. Using premature lambs delivered by Caesarean section, it has demonstrated that dilution of tracheal fluid with amniotic fluid reduces lung compliance and produces respiratory distress.^{2,3} It would seem reasonable, therefore, to postulate that deep gasping respirations in utero as a result of anoxia or cutaneous stimulation near the time of delivery might cause inhalation of amniotic fluid diluting the fetal lung fluid and producing lowered surfactant concentration.

A clear deficiency of surfactant activity and extractable phospholipids has been demonstrated repeatedly in the lungs of babies dying of hyaline membrane disease as well as the lungs of most pre-

mature babies whose birth weight is below 1200 grams. A good correlation between surfactant activity and susceptibility to hyaline membrane disease has been found in premature lambs delivered by Caesarean section.⁸ Glucocorticoids have been found to induce surfactant production by alveolar epithelial cells in immature fetuses. Administration of glucocorticoids 24 hours prior to delivery of markedly premature lambs or human infants prevents the development of hyaline membrane disease. Parenthetically, administration of glucocorticoids after delivery has no beneficial effect on the course of the disease.^{9,10,11}

Pulmonary blood flow in the fetus in utero is controlled by tonic constriction of the pulmonary arterioles. By shunting blood through the foramen ovale and ductus arteriosus, this allows both the right and left ventricles to contribute to cardiac output, thereby increasing blood flow through the placenta. Intrauterine asphyxia, by lowering arterial oxygen, causes even greater pulmonary arteriolar constriction as a mechanism to increase placental flow to counteract the anoxia. Aeration of the lungs at birth causes a dramatic drop in resistance to blood flow through the lungs in mature lambs. This effect is considerably diminished in immature lambs. Anoxia and atelectasis cause a return of pulmonary arteriolar constriction which can be temporarily reduced by injection of acetylcholine.^{2,3,12,13} Treatment of infants with established hyaline membrane disease with acetylcholine produces a temporary dramatic improvement in pulmonary blood flow, arterial oxygen, and many clinical features of the disease including tachypnea and grunting respiration. This improvement is greater than that produced by inhalation therapy with aerosolized dipalmityl lecithin, a major component of pulmonary surfactant, which somewhat improves pulmonary compliance but does not improve oxygen uptake by the lungs.¹⁴ Autopsy studies of lungs from babies dying of hyaline membrane disease show intense pulmonary arteriolar vasoconstriction which remains even days after death.¹⁵ Infants of diabetic mothers who are more prone to hyaline membrane disease than normal infants show significantly diminished pulmonary blood flow as compared with normal infants even in the absence of respiratory symptoms.¹⁶ A case of hyaline membrane disease has been reported in which a sequestered portion of lung which received its blood supply only from the aorta did not show hyaline membrane disease as did the remainder of the lung.¹⁷ It is of interest that some peptides released from fibrinogen during conversion to fibrin (fibrinopeptides) are capable of producing intense prolonged pulmonary arteriolar vasoconstriction with loss of pulmonary compliance.¹⁸

The mechanism of hyaline membrane formation is still unknown. Membranes are never seen in still-

born infants, require a period of air breathing prior to their formation and form only in parts of the lung which have been aerated. In humans they are seldom seen in babies dying less than five hours after birth. When seen at this time, they consist of easily recognizable alveolar epithelium undergoing degeneration but in babies living longer the membranes become more homogeneous with less conspicuous cellular elements and can be shown by fluorescent antibody technique to contain plasma elements including fibrin. Electron microscopy at this stage shows autolyzed cellular debris admixed with amorphous and fibrillar material and there may be defects in the underlying basement membrane which separates the alveolar epithelium from the pulmonary capillaries. In normal infants, the Hale stain demonstrates a thin layer of mucopolysaccharides lining the surface of the alveoli. This material is generally absent in lungs of infants dying of hyaline membrane disease except in the hyaline membranes themselves which often show a strongly positive Hale stain.^{2,3,4,15} Similarly fluorescent antibodies against foam purified pulmonary surfactant show striking localization of antigen in hyaline membranes and marked depletion of the antigen on the surfaces of intact alveolar epithelium.¹⁹ Light and electron microscopic studies on premature infants living less than four hours show a distinctive acidophilic necrosis of alveolar epithelium often associated with partial detachment of epithelium from the basement membrane which can occur within a few minutes of birth following a few gasping respirations or after artificial ventilation.²⁰ Similar rapid changes in the epithelium have been observed within five minutes after artificial respiration of premature Rhesus monkeys delivered by Caesarean section.²¹ Clinical recovery from hyaline membrane disease is paralleled by regeneration and functional recovery of the damaged alveolar epithelium.²² In view of these findings together with the failure of glucocorticoids to affect the disease after it is established, it would seem important to initiate treatment before the alveolar epithelium has been damaged.

Returning to my initial hypothesis regarding the development of hyaline membranes, I think it is reasonable to postulate the following sequence of events.

1.) There may be a deficiency of pulmonary surfactant in the fetal lung fluid at the time of birth. This could be a result either of immaturity of the lung, prolonged inadequate pulmonary blood flow as a result of intrauterine anoxia, endocrine factors delaying surfactant synthesis or by dilution of fetal lung fluid by deep inhalation of amniotic fluid which in some cases might contain substances antagonistic to surfactant activity.

2.) This deficiency may prevent the great major-

ity of terminal alveoli from becoming aerated during initial respiration causing the alveolar ducts to become overdistended especially during inspiration or artificial respiration. Repeated shearing forces on the epithelium may tear the epithelium off the basement membrane resulting in liberation of membrane enclosed hydrolytic enzymes which in turn would produce rapid enzymatic cell degradation. Associated damage to the basement membrane would permit entrance of plasma elements including fibrinogen and other clotting factors which admixed with lung thromboplastin (? identical with elements of pulmonary surfactant) would produce fibrin and inactivate pulmonary surfactant. Once formed these membranes would continue to absorb and inactivate residual surfactant. Pulmonary arteriolar vasoconstriction might be enhanced by release of fibrinopeptides during conversion of fibrinogen to fibrin.

3.) Since the disease is theoretically reversible before epithelial injury develops, it might be possible to prevent the disease by intratracheal administration of surfactant at the moment of birth before or during initial respiratory efforts. Needless to say such studies should be carried out in experimental animal models before consideration of human trials.⁴ Also, since relatively poor results have been observed following administration of aerosolized pure dipalmityl lecithin^{14,23} and membranes contain other components of surfactant,^{3,19} a trial with surfactant of natural origin might be more likely to be effective.

There are, however, other possible pathogenetic mechanisms against which this approach might not be effective. For example, adult hyaline membrane disease or respiratory distress syndrome which except for the patterns of atelectasis resembles hyaline membrane disease of the newborn can be produced by a variety of conditions associated with intravascular coagulation. An excellent model can be produced in dogs by intravenous administration of thrombin in which there is produced atelectasis, hyaline membrane formation, and loss of lung compliance and pulmonary surfactant activity.²⁴ Serum from cord blood of infants who develop respiratory distress contains elevated concentrations of a fibrinogen split product.¹⁸ Entrance of thromboplastin from the endometrial lining or placenta into the fetal circulation conceivably might initiate such a process. In the model of experimental hyaline membrane disease in Rhesus monkeys previously mentioned,²¹ an antigen was found within the beginning hyaline membranes which reacted with fluorescein-labeled antibody against pepsinogen suggesting the possibility of aspiration of gastric secretions as a pathogenetic mechanism. It is also of interest, although not antagonistic to my hypothesis, that it has been shown that premature human infants lack serum plasminogen and that administration of plas-

minogen to infants at the time of birth significantly reduces the severity and increases survival in hyaline membrane disease.²⁵

In summary, shearing of alveolar duct epithelium from the underlying basement membrane appears to be a reasonable explanation for the formation of hyaline membranes in hyaline membrane disease of the newborn, the disease may be much more difficult to treat once this has occurred, and it is at least conceivable that the disease may be averted by prophylactic administration of pulmonary surfactant intratracheally at the time of birth. However, since there are other possible pathogenetic mechanisms and since there may well be practical difficulties in appropriate administration of surfactant, no conclusions can be reached until experimental trials have been conducted.

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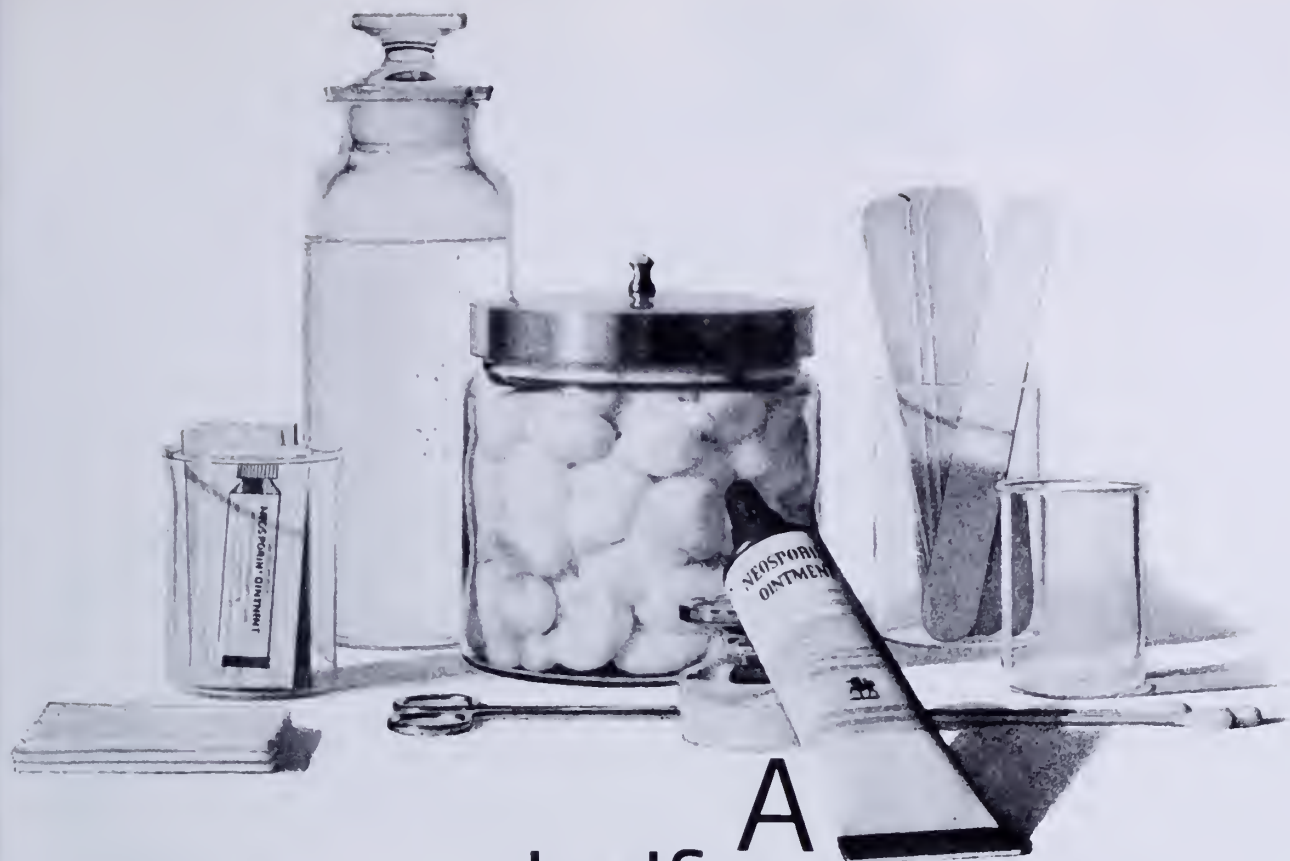
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Actinomycosis

WILFRED GUERRA, M.D.*

Four cases of actinomycosis were diagnosed and treated in a seven-year period at the Veterans Administration Center, Togus. The site of involvement was different for each one. Penicillin was the antibiotic of choice, combined with appropriate adjunctive surgery. Recovery occurred in all cases, with no relapse or recurrence to date.

MATERIAL AND METHODS

The first case in this group appeared in 1968 as pleuropulmonary actinomycosis and it was reported in detail by Turner.¹ In the second case, intra-abdominal infection recurred following an appendectomy. The third patient presented with chronic infection in the left sub-maxillary region. The last case was seen recently for perianal inflammatory swelling.

Identification was based on morphological characteristics, Gram-positive non-sporulating organisms, and also on culture requirements, enriched nutrient broth under anaerobic conditions. A single "sulfur" granule was recovered from the last patient when an abscess was drained and it presented typical microscopic features.

CASE REPORTS

Case 1: L.D., a 51-year-old male, was admitted April 16, 1968 because of pain in the chest, cough, and general symptoms of chills, fever, and malaise. Chest x-rays showed two air fluid levels at the right base and a small area of density in the upper right lung field. From the purulent material obtained by thoracentesis of the pleural empyema, *Actinomyces israelii* were demonstrated microscopically and by cultures. Drainage was accomplished by a closed thoracotomy and large doses of penicillin were administered. Treatment also included irrigation of the pleural cavity with penicillin solution. The lung density resolved. The empyema diminished considerably when Lipiodol was injected into the chest tube and a bronchopleural fistula was demonstrated. Penicillin was continued until the fistula had closed.

Case 2: L.S., a 23-year-old male, was admitted August 8, 1970 complaining of a painful lump in the right groin of two weeks' duration. The pain became worse and he felt feverish the day before admission. The past history was significant for an appendectomy in February of 1966 and ten months later a right inguinal herniorrhaphy was done while in Viet Nam. A painful lump appeared in January 1970 at the right groin similar to the present illness. He was admitted at that time for a possible recurrent hernia but at surgery an abscess was found and drained. Cultures revealed no growth and recovery was uneventful.

Examination on this admission revealed a young male in slight distress. His temperature was 99°. The heart was normal and the lungs were clear. The abdomen was flat and soft and there were two transverse scars in the right lower quadrant. In relation to the lower scar there was a tender lump approximately 3 cm. in diameter, non-reducible and non-fluctuant. The white blood

count was 13,680 with 79% neutrophils, 18% lymphocytes, 2% monocytes, and 1% eosinophils. Urinalysis was normal. The chest x-ray was negative.

The abscess ruptured and drained spontaneously during the night with relief of pain and a drop in body temperature. Drainage of mucopurulent material continued at the sinus tract opening that formed in the middle of the lower incisional scar. Repeated cultures showed no growth. Later, a probe was passed through the oblique tract into the abdominal wall. The tract was visualized in a sinogram but it did not enter into the peritoneal cavity or bowel. A barium enema was reported to be within normal limits.

On August 18, 1970, the sinus tract was excised. It appeared to taper and end at the peritoneal layer. However, at that point a small opening was found that led into a loculated intraperitoneal abscess 2 to 3 cm. in diameter which was drained and its purulent contents were cultured. The abdomen was sutured in layers with a Penrose drain in the abscess cavity. The drain was removed on the third day and that night the wound area became painful and the temperature rose to 103°. Lincomycin was given empirically and in 48 hours the pain and temperature subsided. Skin sutures were removed on the usual seventh day and the incision was healing and clean. One week later the culture growth was reported positive for *A. israelii*. Large doses of intravenous penicillin therapy was started. A generalized faint erythematous drug rash developed during the fourth week of treatment which was controlled by Benadryl.[®] The antibiotic was discontinued Oct. 15, 1970.

Case 3: J.S., a 43-year-old male, continuously hospitalized for chronic schizophrenia for the past ten years, was seen in consultation Dec. 3, 1971 for swelling in the left submaxillary region which began three weeks before and which now started to bother him. He smoked up to three packages of cigarettes per day. The mass was ill-defined and non-tender. The ears, nose, and throat were not remarkable. The teeth were in fair repair and the gums were not inflamed. The tongue was coated and the buccal mucosa appeared intact. No nodules were palpable in the floor of the mouth and there was no cervical node involvement. The heart was normal and the lungs were clear. The abdomen was flat and soft.

More diagnostic work-up was requested. X-rays of the paranasal sinuses showed good visualization with no evidence of facial bone destruction. The hypopharynx and larynx were described as within normal appearance.

There was no dental condition present to account for the swelling. However, it was noted that the left lower third molar was extracted six months earlier. X-ray films of the mandible showed the tooth socket filled with new bone and the rest of the mandible free of disease.

On Dec. 25, 1971, the pain became worse. The body temperature ranged from 100 to 101.2°. The white blood count was 12,300 with 87% neutrophils, 10% lymphocytes, and 3% monocytes. A urinalysis was negative. The chest x-ray was negative. Ampicillin was started and the next day he was transferred to the Surgical Service. Examination at this time revealed the swelling slightly increased, measuring 6x3 cm. and more tender but no skin redness was noted.

Two days later he was taken to the operating room. The swelling was aspirated first with a needle and syringe. About 15 cc. of grayish yellow pus was obtained and sent directly to the laboratory in the syringe for cultures. The inflammatory mass was incised and drained. The ampicillin was continued post-operatively. By Jan. 7, 1972, the cultures had produced a growth

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TABLE 1

SUMMARY OF ACTINOMYCOSIS CASES					
Admission date, sex, age	Diagnosis	Possible source or route of invasion	Time lapse	Antibiotic therapy (duration)	Adjunctive surgical treatment
Case 1 4/16/68 L. D. M 68	Pleuropulmonary actinomycosis	Break down of small lung abscess	2 weeks	1-V aq. penicillin 20 M units/day/63 1-M proc. penicillin 2.4 M units/day/21 (12 weeks)	Closed thoracotomy with under-water seal tube drainage. Irrigation of pleural cavity with 2 M units penicillin daily.
Case 2 8/8/70 L. S. M 23	Intra-abdominal abscess — <i>A. israelii</i>	Previous appendectomy	4½ years	1-V aq. penicillin 6 M units/day/51 (6½ weeks)	Excision of abdominal wall sinus tract; drainage of intra-abdominal abscess. (8/8/70)
Case 3 12/3/72 J. S. M 43	Submaxillary actinomycosis	Tooth extraction	6 mos.	1-V aq. penicillin 20 M units/day/32 (3½ weeks)	Incision and drainage. (12/27/72)
Case 4 12/19/74 G. J. M 48	Perianal abscess (actinomycotic) Diabetes mellitus	Anorectal crypts	5 years	1-V aq. penicillin 2- M units/day/16 12 M units/day/13 (4 weeks)	Incision and drainage (12/20/74)

of *A. israelii*. The treatment was changed to large doses of intravenous penicillin. The inflammation resolved gradually and treatment terminated Feb. 18, 1972.

Case 4: G.J., a 48-year-old male, known diabetic, allegedly controlled by diet alone, was admitted Dec. 19, 1974 complaining of pain and swelling on the left side of his anus which began four or five days before admission. A similar illness had occurred five years previously which required incision and drainage.

The physical examination was not remarkable except for a moderately tender, reddened swelling left of the anus. A small opening was present to the inflamed skin zone just lateral to the anal orifice from which a small amount of mucopurulent material drained.

The white blood count was 6,665 with 64% neutrophils, 28% lymphocytes, and 8% monocytes. A urinalysis showed the specific gravity to be 1.032, a 4+ glucose, 4+ ketone, and a trace of protein. The blood sugar determination was 271 mg.

Under anesthesia the next day, examination revealed induration of the left anal wall contiguous with the reddened perianal swelling. A probe into the skin opening led into a small superficial abscess cavity. Then the incision was made through the skin opening in a radial plane to the anus. No internal opening was present. However, a small pale yellow granule 2 to 3 mm. in diameter was found in the abscess cavity. This was sent to the laboratory with a specimen of bloody purulent material for culture with sensitivity studies. The abscess cavity was packed lightly with a strip of iodoform gauze. Sitz baths were started the next day and the gauze strip was removed. The diabetes was stabilized with regular insulin based on 4-way urines. On the third postoperative day, he was discharged from the hospital upon his insistence (Dec. 23, 1974).

Slide preparations made of the tiny granule were stained with methenamine silver nitrate. Masses of Gram-positive filaments that were surrounded by inflammatory cells were observed microscopically (Figure 1). Other sections were stained with hematoxylin and eosin. These findings of the "sulfur" granule were typical of Actinomyces.

The patient was convinced to accept readmission and penicillin therapy was begun Jan. 27, 1975. At that time, examination of the anus showed a non-tender linear scar 2 cm. long corresponding to the recent incision. It was not completely bridged by epithelium and there was a band of induration at the base. He received a course of intravenous penicillin via a heparin lock needle and it was terminated on Feb. 26, 1975 at which time he again wished to be discharged. The inflammation was gone com-

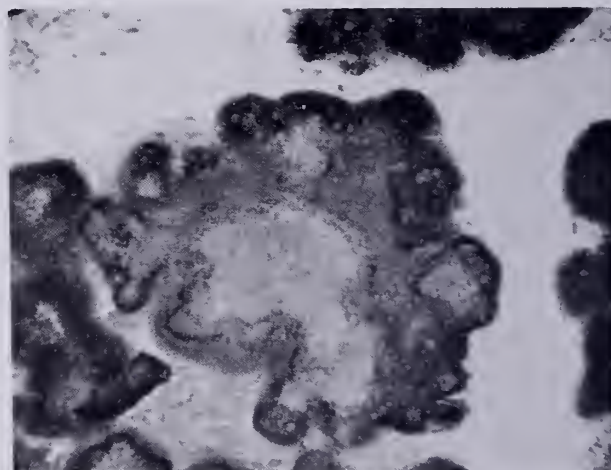


Fig. 1. View of "sulfur" granule from Case 3. (Methenamine silver nitrate stain, X75)

pletely. On leaving, he volunteered the information that he felt completely free of discomfort for the first time since his illness began five years previously.

These four cases are summarized in Table 1.

COMMENT

Actinomyces israelii, a Gram-positive non-sporulating organism, requires enriched culture media for growth (thioglycolate or brain-heart infusion) and anaerobic or microaerophilic conditions. Growth is slow in culture but it may be enhanced under carbon dioxide. This organism is usually mixed with other organisms which grow more rapidly and therefore the culture material should not be discarded too early. Fastidious requirements and slow growth are characteristic properties which make diagnosis difficult. When possible, the specimen for culture should be collected as fluid aspirate

as in Case 3, J.S., and appropriately transported to the laboratory.²

Infections with *A. israelii* are endogenous. It is not unusual to find the organism in the tonsillar crypt, scrapings of teeth and gums, and in the gastrointestinal tract (appendix³ and anorectal region⁴). Trauma, disease, or surgical manipulation is essential for invasion of tissue by these organisms. Sometimes the infection may remain dormant for a long time (years) as suspected in Case 2, L.S., and Case 4, G.J. Actinomycosis is characterized by chronic, destructive abscesses of connective tissue which eventually penetrate through the skin or into adjacent viscera resulting in sinuses or fistulae. Lymphatic spread does not occur but dissemination through the blood stream is possible.

Actinomycotic pus⁵ consists of typically dense infiltration of inflammatory cells, mainly polymorphonuclear leukocytes, in the center of which are colonies of *Actinomyces* which present as "sulfur" granules. The colonies are imbedded in a matrix of calcium phosphate⁶ and the center consists of central filamentous mycelia with characteristic clubbing that presents a radiating pattern (hence "ray fungus"). The filaments may be branched and stain Gram positive. The clubs at the tips of the mycelia are not spores but are deposits of host lipid⁷ which may stain Gram negative.

CONCLUSION

Actinomyces israelii is sensitive to penicillin,

tetracycline, chloramphenicol, streptomycin, and clindomycin. Adequate surgical drainage, resection of damaged tissue, and excision of sinus and fistulous tracts are necessary adjuncts to antibiotic therapy. Penicillin given intravenously in large doses has been one treatment of choice. It was well tolerated by all four patients with the exception of Case 2, L.S., who developed a generalized drug rash. Treatment with Benadryl was prescribed and he was able to complete the penicillin therapy. The four cases presented show no actual uniformity in doses of intravenous penicillin used. The longest duration of therapy was approximately three months in Case 1, L.S. It has also been suggested to continue penicillin therapy for a period of six months to one year longer.⁸ The generally accepted recovery rate is around 90%.

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PELVIC LIPOMATOSIS — Continued from Page 179

leading to uremia unless some surgical measures are taken when and if possible. Complete extirpation of the fat from the pelvis is considered unattainable. It appears to be more common in blacks and there is only one report in a woman. Prognosis is poorer in the younger patients. Hypertension may be present. The etiology is not known.

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Maine Blue Cross and Blue Shield News

CONSUMER UNION CITES NHI GOALS

Building on the strengths of the present private insurance system is a reasonable approach to a national health insurance program, maintains the Consumers Union (CU), a national consumer group.

A recent article in *Consumer Reports* evaluated "five major" NHI prototypes before Congress in relation to consumer goals. In absence of the ideal consumer bill, CU sees a most "reasonable approach" built on the private insurance system.

While using the insurance system's identity, organizational structure, buildings and staff, the consumer group said an independent government watchdog should monitor carriers.

Then, the article stated, if the carriers fail to meet specified goals for consumer representation and responsiveness, claims efficiency and cost control, they should be phased out gradually "in favor of total government administration."

According to the publication, there's reason to believe the new Congress will pass a national health insurance bill, but it "will fail to meet many of the stated consumer goals."

Consumer Goals

In CU's viewpoint, NHI must meet five minimum goals in the consumer's interest:

- It should be comprehensive, mandatory with the entire population covered.
- There should be no connection between a patient's income and the extent of quality of medical care.
- Financing should be raised through a form of progressive taxation (those who can afford less should pay less, and those who can afford more, pay more) and in a manner open to public scrutiny.
- The program should provide incentives for efficiency, control over cost and quality of

services, and encouragement of alternative delivery systems in health care.

Program administrators should be accountable to the public, and "consumers should have a voice in administration."

Meeting Objectives

Five bills were discussed in the article — AMA's Mediscore, the Administration plan, the Long-Ribicoff Catastrophic proposal, Kennedy-Mills, and the Kennedy-Griffiths plan. In CU's judgment, only the last two are capable of fulfilling most of the five consumer goals.

Considering the multibillion dollar price tag on the Kennedy-Mills plan, CU added that such figures do not necessarily mean new spending but a regrouping into one program of all the separate programs made for private health insurance premiums, out-of-pocket costs, and Medicare and Medicaid.

The magazine said cost is often an objection raised to a comprehensive Federal plan, but cost, like "socialized medicine," is a scare word.

"However, comprehensive national health insurance would result in additional, rather than just transferred costs, if it generated a new demand for health service," the publication continued.

Controlling Costs

The consumer group said physician fee schedules would be necessary to control costs under a national program, but doctors should be given a choice of participation or non-participation.

Although non-participants could charge any amount, CU recommends that no part of their services be reimbursable under the new program.

"Patients choosing treatment from physicians or other health care providers who decide not to participate . . . would have to pay the entire bill themselves," said the publication.

County Society Notes

ANDROSCOGGIN

The Androscoggin County Medical Association convened its April session on April 17, 1975 at Steckino's Restaurant in Lewiston, Maine. There were sixty members present with Dr. John B. Madigan, President of the Maine Medical Association, as guest. The minutes of the previous meeting were read and approved by the membership without correction.

Dr. Ross W. Green presented a report of the Political Action Committee which was of considerable interest to all members present. To insure that this Association would not run afoul of the legalities of having a Political Action Committee, by vote, which was unanimous, the name of this committee was changed to Legislative Action Committee with same members and same chairman.

Dr. Stanley D. Rosenblatt then presented a detailed discussion of the recent Interim House of 'Delegates' meeting held in Waterville on April 12, 1975. Dr. Herbert J. Wright, Jr., Executive Committee member of the 7th District, then presented his report. There was considerable discussion, particularly surrounding the proposed budget and possible dues increase to the State Medical Association. By vote of the membership, the delegates of the Androscoggin County Association were instructed to vote against a proposed fifty (\$50) dollar increase in the annual dues of the Maine Medical Association. There was considerable discussion concerning this vote and passed by a narrow margin. There also was considerable discussion about the renewed proposal of finding an Administrative Assistant for Dr. Hanley's office. It was the intent of this County's membership to encourage acquisition of aid and assistance for Dr. Daniel Hanley in the form of an Administrative Assistant or Assistant Executive Director for the Maine Medical Association. A unanimous vote of confidence is extended to Dr. Hanley in relationship to his fine representation of the Maine Medical Association, both within and without our fine State.

The Credentials Committee presented application for membership from Dr. George N. Morrisette following receipt of which membership took a unanimous vote, and we welcomed

Dr. Morrisette to the Androscoggin County Medical Association and the Maine Medical Association.

Chairman of the County Medical-Legal Committee discussed the ongoing problems with medical liability insurance and the aid and assistance which is forthcoming from Mr. Hogarty, the Superintendent of Insurance for the State of Maine.

Under new business, there was considerable discussion centering on Blue Cross/Blue Shield, the most volatile of which was the recent mailing from Blue Cross-Blue Shield to its policy holders in relationship to service benefits. It is apparent that there is a great deal of ambiguity in this recent letter and that it has placed an even greater load of aggravation upon the physician's office personnel to explain the presence or absence of service benefits to Blue Cross/Blue Shield contract holders. By unanimous vote, this Association registers extreme displeasure with Blue Cross/Blue Shield for once again placing physicians and their office personnel in the position of explaining a third-party's contractual arrangements with their policy holders. Once again, this type of surreptitious maneuver produces further inroads in the tenuous credibility established between the medical profession and a third-party provider.

A vote of Honor for Dr. Ralph A. Goodwin, Sr. at the time of his retirement from active practice was prepared for the membership. This will appear in the pages of *The Journal of the Maine Medical Association*.

Upon completion of the business for the evening, membership was once again reminded that the next meeting would be May 21, 1975 — the annual Dutch Treat for the wives.

Dr. John B. Madigan, President of the Maine Medical Association, was then introduced by Dr. Rosenblatt, Program Chairman. Dr. Madigan spoke about the direction, both current and for the future, in respect to the current and future legislation, leadership in relation to problems of medical liability insurance, and need for arbitration and bargaining power with third-party providers. A lively question and answer session followed.

The meeting was adjourned at 10:55 p.m.

RICHARD M. SWENGEL, M.D., *Secretary*

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Number 8

Radionuclide Angiocardiology

DEMITRIOS NIKOLAIDIS, M.D.

Radionuclide angiocardiology is the application of radioactive tracer techniques to the evaluation of patients with disease of the heart and blood vessels. It depicts the circulation within the heart, lungs and great vessels. It is simple to perform, results in a very low dose, and does not produce hemodynamic disturbance or pharmacologic effect. The examination can be repeated with practically no risk.

HISTORICAL BACKGROUND

Most physicians assume that the first radioactive tracer studies in diagnostic medicine were of the thyroid. Almost 50 years ago, however, Blumgart and Weiss published a series of papers concerned with the velocity of the circulation in normal persons and in patients with heart disease. When we consider that these researchers used solutions of radon as tracers and a cloud chamber as a radiation detector we can better appreciate the technical advances that have been made since that time.

The first widely used procedure involving radioactive tracers and the heart was developed by Rejali, MacIntyre and Friedell in 1958. They applied the scanning method to visualization of cardiac blood pool in the diagnosis of pericardial effusion. In 1962, Folse and Braunwald reported a method of using radioactive indicator dilution with a single precordial detector and introduction of the radionuclide directly into the left ventricle that permitted estimation of the fraction of the left ventricular end-diastolic volume (EDV) ejected per beat. Since then there have been many attempts to devise a non-invasive procedure for evaluation disorders of the cardiovascular system.

EQUIPMENT AND METHOD

The procedure today requires a gamma scintillation camera which simultaneously records the position and intensity of radioactivity as a function of time. The information thus obtained can be stored on magnetic tape. The patient can be released and later the magnetic tape played back and selective sequential images can be obtained on polaroid, 70 mm or regular x-ray film. On the left side of each image the elapsed time and the sequence of the image appear for orientation. Using a data processing unit the images can be summed, integrated or subtracted in any manner desired. Although the spatial resolution of the cameras is limited, it can provide visual recognition of normal or abnormal patterns. Fig. No. 1 represents images as the tracer enters through the superior vena cava, the right atrium, right ventricle, pulmonary artery, perfuse the lungs and returns to the left side of the heart outlining finally the aorta and its major branches. Images can also be obtained with different degrees of summation or subtraction to depict the different parts of the cardiopulmonary cycle (Fig. No. 2). On these images we can, not only evaluate anatomical changes, but by using the simultaneously recorded time we can roughly estimate transit or peak to peak time. This procedure represents the qualitative radionuclide angiocardiology.

The gamma camera can be interfaced to an on line digital computer or as in our department to a programmable calculator in conjunction with the data processor. After viewing the entire examination, "areas of interest" are placed over region of special interest like the superior vena cava, the right or left ventricle or atrium, right or left lung. Within a few seconds time-activity curves can be generated and can be analyzed qualitatively and quantitatively. This represents the Quantitative Radionuclide Angiocardiology.

From the Department of Radiology and Nuclear Medicine, Augusta General Hospital, Augusta, Maine 04330.

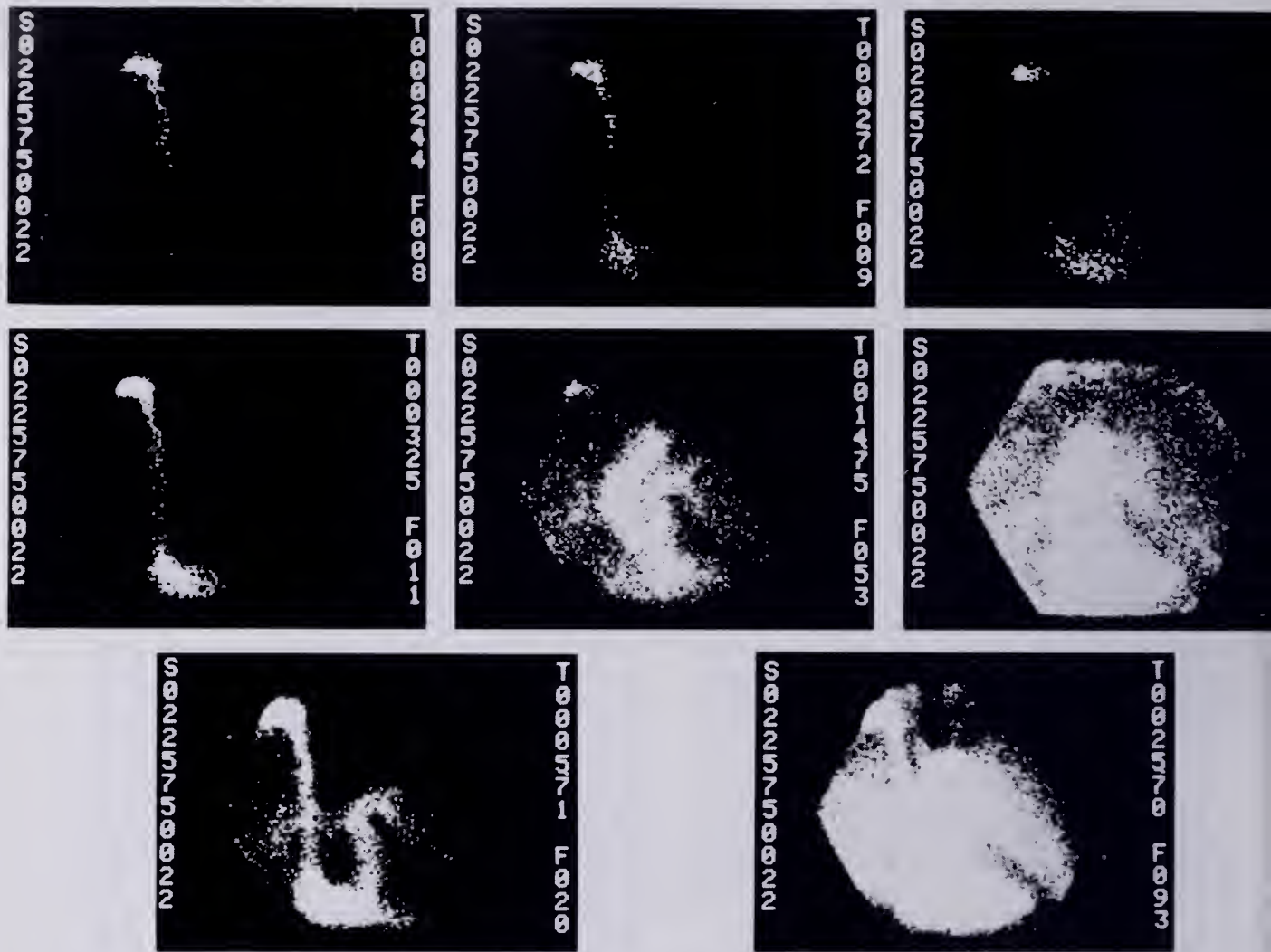


Fig. 1. Imaging of a normal cardiopulmonary cycle. Injection in the right antecubital vein.

The camera or the patient or both are positioned so that anteroposterior or oblique views are obtained according to the desired information. The radioactive material most commonly used is the ^{99}M Tc Sodium Pertechnetate, available at all times in small community hospitals, and is rapidly injected in a less than 1 ml volume bolus and in a dose of 200 $\mu\text{Ci/kg}$ body weight. For cardiac output determination, human serum albumin is tagged with Tc 99m in a solution of high specific activity (20 to 40 m Ci/ml).

CLINICAL APPLICATIONS OF THE PROCEDURE

Congestive Heart Failure — By far the most common cause of an enlarged radiographic cardiac silhouette is congestive heart failure. Unlike with pericardial effusion, the intracardiac blood pool is enlarged without an increase in the space between the intracardiac blood pool and the adjacent vascularized organ. Unlike with left ventricular aneurysm, cardiac enlargement is more generalized,

usually involving multiple chambers, and there is no focal dilatation involving portions of the ventricular wall. Examination of the cardiopulmonary bolus passage reveals that (1) the transit time is prolonged, (2) the ejection fraction (EF) is low, and (3) the shape of the bolus through the ventricle is flattened and is like a dome rather than a peak.¹ Although these quantitative parameters are nonspecific, they are helpful and objective. They are particularly helpful in documenting the efficiency of medical therapy for congestive heart failure. It has been found that changes in the transit time more clearly and objectively correlate with the medical course than changes seen on the radiograph, which sometimes lag behind clinical improvement.

Left Ventricular Aneurysm — Demonstration of the left ventricular cavity by the radionuclide bolus usually reveals generalized enlargement as well as a more focal bulge. These focal areas usually demon-

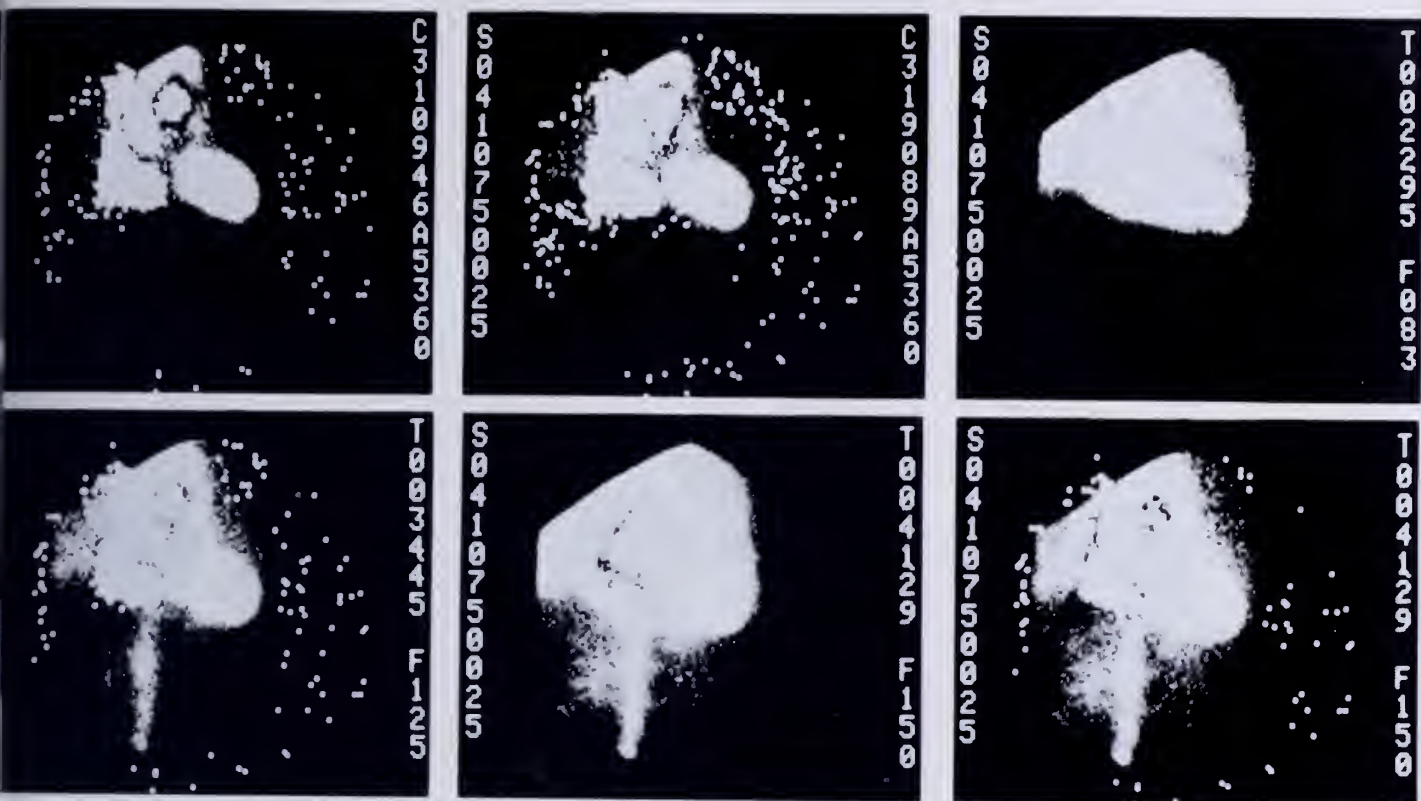


Fig. 2. Summed and subtracted images to depict the left side of the heart and aorta.

strate prolonged residence of the radioactivity in the involved region because of stagnant flow. Further evaluation of the localized dilatation in systole sometimes demonstrates a paradoxical motion that can be used to confirm an aneurysm. With an ECG gating system, images corresponding to systole, can be summed and compared to a composite image of diastole. Areas of paradoxical motion or akinesia can be separated from the normal myocardial movement. Since these complications of myocardial infarction are not very uncommon, the importance of evaluating these most important parameters of actual myocardial damage and the ability or inability of the cardiac muscle to perform becomes obvious.

Evaluation of Valvular Lesions — Stenotic or regurgitant valvular lesions can often be recognized as abnormal changes on the radionuclide angiogram. Although the anterior view is useful, the RAO view is preferred for lesions of the tricuspid, pulmonary, and mitral valves. Sometimes, however, mitral lesions cannot be identified if the patient is in congestive heart failure and the LAO or left lateral view may be best. The LAO or left lateral view is also preferred for studying the aortic valve. See Fig. No. 3 where the markedly enlarged left atrium, mildly enlarged left ventricle, and relatively hypoplastic aorta prolongation of circulation time and prominence of the pulmonary outflow tract are

seen on a case with mitral valvular disease.

Aortography, Arteriography and Venography —

The aorta and its major branches can be well imaged and studied after intravenous bolus injection of the tracer to rule out obstructing lesions, aneurysms or other congenital or acquired anomalies. Fig. No. 4 shows right aortic arch. Compare these images with the normal. The tracer was injected in the left antecubital vein.

Distribution of perfusion in the extremities can be determined during peripheral arteriography in intra-arterial injection of labeled albumin particles or microspheres of albumin. Diffuse disease of the vessels is indicated by a generalized decrease in blood flow to muscle as compared to skin; stenotic lesions of large vessels cause regional decreases in activity. Healing of skin ulcers can often be predicted on the basis of the degree of associated hyperemia. Quantification of the size of arteriovenous fistulae can be made through measurement of pulmonary activity after arterial injection of microsphere. Increased sensitivity of the method can be achieved by injecting microspheres during reactive hyperemia resulting 5 — 15 s after injection of radiographic contrast media.

Radionuclide venography of the legs and pelvis is performed by injecting labeled albumin particles or microspheres into a foot vein and monitoring them

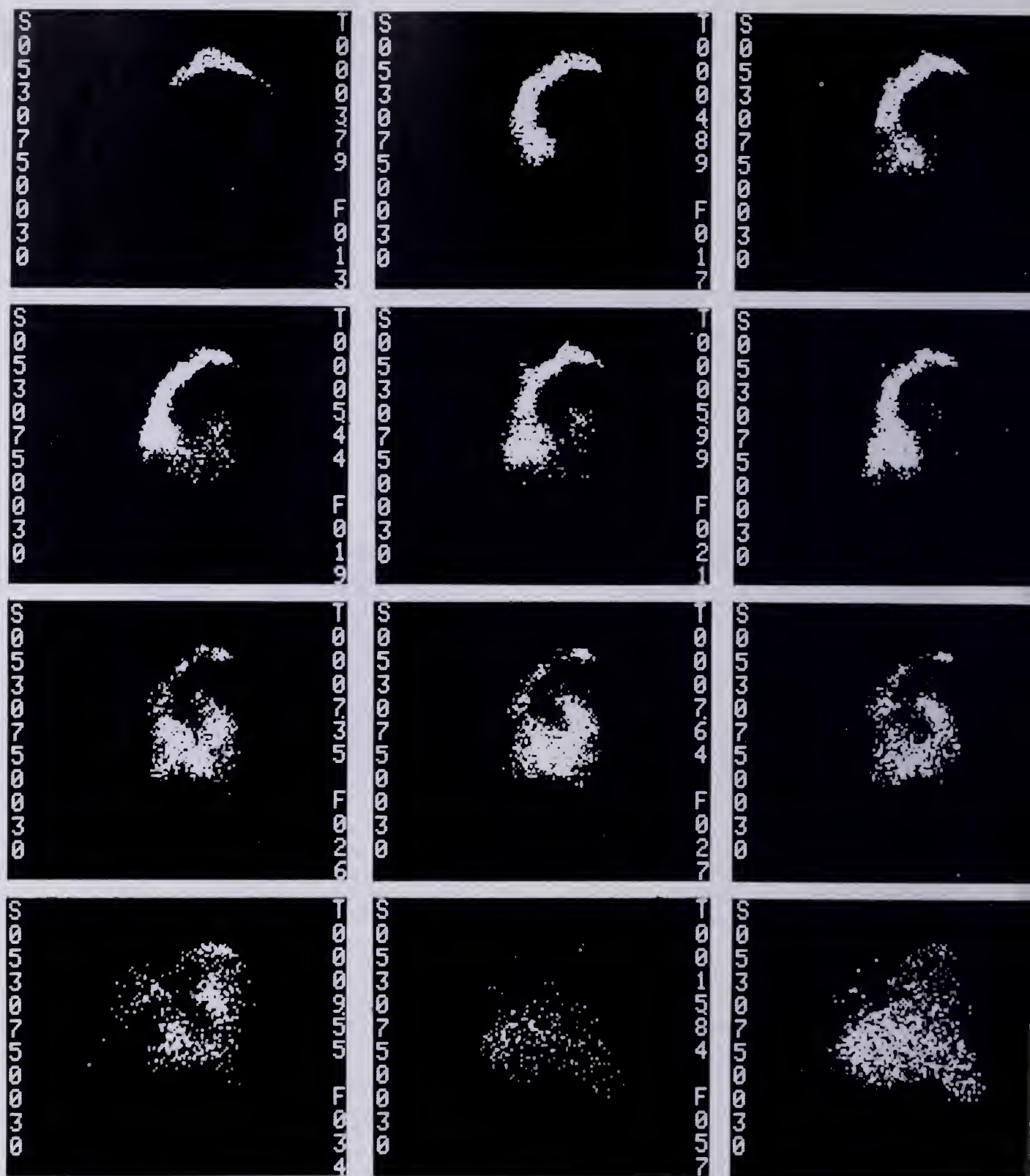


Fig. 3. Injection in the left antecubital vein. Note in frames 5 and 6 small reflux of activity in the right innominate vein and inferior vena cava. Also note prominent outflow tract of the right ventricle, markedly enlarged left atrium and slight enlargement of left ventricle as seen in mitral valvular disease.

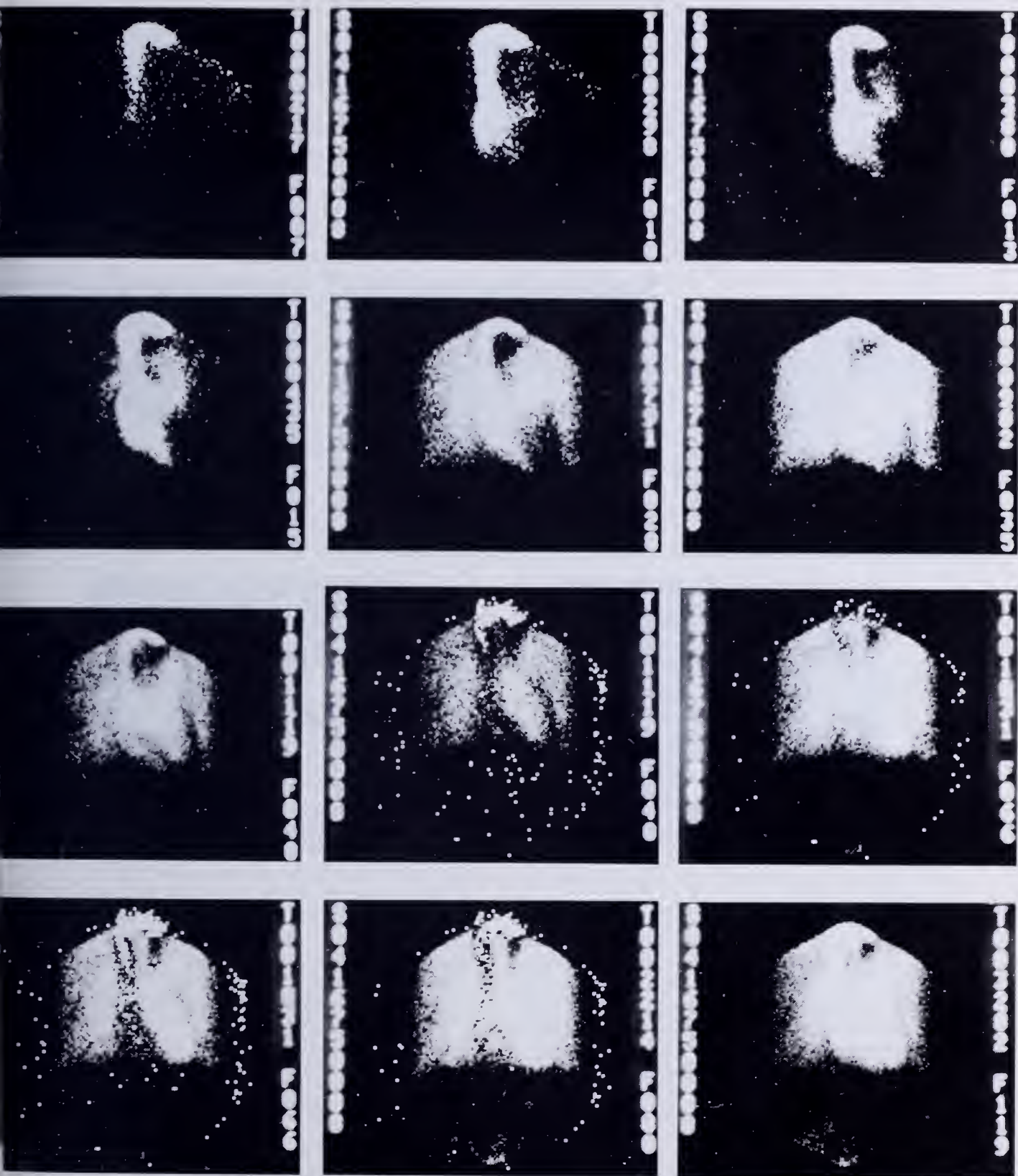


Fig. 4. Injection in the left antecubital vein. Manipulated images. Note right aortic arch.

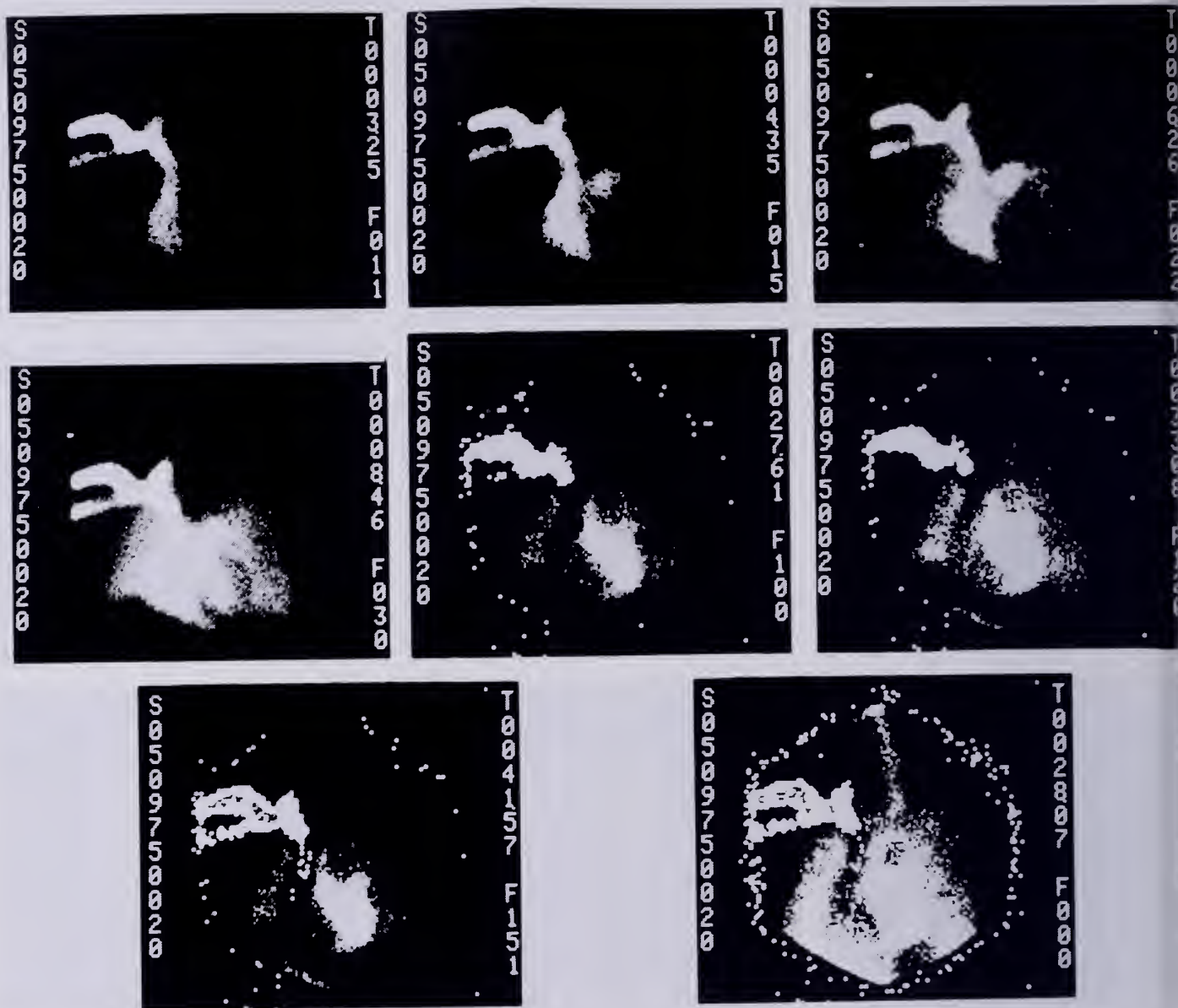


Fig. 5. Injection in the right basilic vein — summed and subtracted images. Note complete absence of recirculation in the right heart excluding left to right shunt.

as they ascend the leg into the inferior vena cava. An obstruction with collateral flow can be determined if serial scintigrams of the area can be done to evaluate the presence of thrombi. Particles of albumin adhere to thrombi indicating their presence and location. This procedure can be combined with lung scanning to detect silent infarction which can be as high as 60% of cases with abnormal venogram.

Intracardiac Shunts — Right to left shunts are detected by early visualization of the radioactive indicator in the aorta either before or at the same time as the tracer appears over the lung fields. By careful visual inspection, the site of the shunt can be determined.

With a shunt at the atrial level (tricuspid atresia, Ebstein's anomaly, and critical pulmonary stenosis or pulmonary atresia with intact ventricular septum) the radionuclide is seen first in the left atrium, and subsequently in the left ventricle and aorta.

With a shunt at the ventricular level (tetralogy of Fallot, pulmonary atresia with ventricular septic defect, transposition of the great vessels without ventricular septic defect and Eisenmenger's syndrome) the radionuclide appears in the left ventricle and aorta following visualization in the right ventricle.

When the shunting is between the pulmonary artery and aorta, the tracer appears early over the aorta but not the left atrium or left ventricle. This

pattern is seen in patent ductum arteriosis with reversed flow and in transposition of the great vessel with an intact ventricular septum.

Left to right shunting can be diagnosed by visual analysis and evaluation for detection of reappearance of activity in the right side. Fig. No. 5 shows no such reappearance in the right side on the manipulated images thus excluding suspected left to right shunt.

Evaluation of Cyanotic Newborn Infants — It is very helpful in making the diagnosis of transposition with right to left shunt by seeing the tracer in the aorta and no activity in the lung fields. On the other hand in pulmonary disorders the angiograms may be normal. In cases of increased pulmonary vascular resistance, we may see a right to left shunting through a patent foramen ovale or patent ductus arteriosis or both. However, the lungs still show greater radioactivity than in transposition. This technique is very simple and quite safe in seriously ill newborn infants unable to tolerate cardiac catheterization.

Evaluation of Cardiovascular Surgery — Radionuclide angiocardigraphy is useful in evaluating the postoperative period, shunt closure, recurrence of ventricular or atrial septal defect and patency of different types of anastomoses.

Cardiac Output — Radioisotope tracers have not been widely used for measurement of cardiac output during catheterization procedures because they offer no significant advantage over nonradioactive tracer dyes, which can be accurately measured spectrophotometrically. They have proven very valuable, however, when they are used in conjunction with other radiotracer studies, such as radionuclide angiocardigraphy; also, their short physical half-life facilitates serial determinations, since radioactive tracer levels in the blood do not continue to rise as do tracer dye levels. These measurements can be incorporated in the total package of studies of heart function using tracer methods.

Cardiopulmonary Transit Times — Treves, Lange, and Freedman⁴ studied cardiopulmonary hemodynamics using an analysis of the $^{99m}\text{TcO}_4$ — dilution curves obtained from patients without evidence of cardiopulmonary disease who were referred for brain scan. Times between peak radioactivity levels over selected areas are as follows: RV to lungs, 2.8 — 0.3 sec; lungs to LV, 3.9 — 0.4

sec; RV to LV, 6.1 — 0.5 sec.⁴ Examples of prolonged circulation times were found in cases of congestive heart failure, valvular disease, and myxoma of the mitral valve. Additional experience has shown that transit time as high as 30 sec can be encountered. Although most cardiac diseases prolong the transit time, reduced values can be encountered in children and patients with tachycardia, thyrotoxicosis, and pulmonary embolism.¹

Ejection Fraction — There are several different methods of estimating left ventricular ejection fraction by radionuclide angiocardigraphy. It represents a very valuable parameter of left ventricular function.

Quantitation of Shunts — Left to right shunts can be detected and quantified by analysis of time activity curves generated from the lungs and providing pulmonary to systemic flow ratios (Q_p/Q_s) directly. It is reported that, in general, quantitative analysis of shunts gives values of shunt size within 10% of value obtained at cardiac catheterization.

SUMMARY

The radionuclide angiocardigraphic study in which the intravenous bolus injection of ^{99m}Tc -pertechnetate or albumin tagged with ^{99m}Tc are used is a safe and valuable method of evaluating cardiovascular disease. Because the procedure is simple, it also lends itself to repeated follow-up studies permitting evaluation of the effectiveness of therapy and follow-up of the course of progressive cardiovascular disease. It represents a very useful diagnostic tool and its clinical application should expand as its potentials become more known to physicians.

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Central Maine Family Practice Residency

Fourteen Months of Patient Care in the Model Practice Unit

ALEX JEROME, M.D.*

BACKGROUND

The Central Maine Family Practice Residency has been discussed previously in the Journal.¹ Within the framework of the Residency stands the Family Medicine Institute. It is in the model practice unit that the residents and staff are on the front line of medical care. We deliver primary care in the field of medicine, surgery, pediatrics, psychiatry, and obstetrics-gynecology. The practice consists of approximately 3,600 patients of whom 93% are private patients and 7.0% are clinic patients from the Augusta General Hospital. This article will discuss the common illnesses encountered by the residents and staff in this population over a 14-month period. There will also be a discussion about the age-sex breakdown of our practice.

METHODS

Essential to collection of data in family practice is a device called the diagnostic index E-Book. This system was originally developed in England.² At the Family Medicine Institute we have modified the diagnostic E-Book into a series of index cards. These index cards are numbered with a classification number and are placed into an easily accessible file system. After each patient is seen, the physician determines the diagnosis or symptom and records the appropriate code number from the classification onto an encounter form. The secretary then transfers the code number to the diagnostic index. The code number itself is derived from the International Classification of Health Problems in Primary Care. The Central Maine Family Practice Residency took part in the development of this classification through participation with over 300 other practices in nine different countries in 1974. The development and acceptance of this classification system has been detailed elsewhere in the literature.³⁻⁵ The International Classification of Health Problems in Primary Care or ICHPPC System is now available for use by family physicians and other primary care providers, including pediatricians, internists, and obstetricians-gynecologists in their office practice.¹

An age-sex register is also essential to the re-

trieval of data in a primary care setting.⁶ Utilizing the register, an exact tally can be kept at all times of the breakdown of the practice concerning age and sex.

FINDINGS

Data was collected on our patients over a 14-month period from January 1974 until March 1975. Table 1 reveals an analysis of our practice by age group, and sex.

Our age-sex analysis in our practice reveals a relative excess of patients in the 15 to 24 age group. This is useful in the fact that our physicians would benefit particularly from training in contraceptive techniques. With a large amount of patients in the 25 to 34 age group, the physicians in our practice should have a healthy emphasis on obstetrics and gynecology. Another use of the age-sex register would be in outreach. It is recommended that members of the 65-year-old and over population have influenza vaccine. In this register we have the capacity to do this. In the field of peer review and audit, our register enables the staff member to randomly audit the charts of three-year-old children in order to determine if adequate immunization has been done.

Next we are concerned with the types of health problems we deal with in the Family Medicine Institute. Table 2 gives the 30 most common problems encountered in our practice. It is to be noted that every visit for these problems is recorded. This will account for the position of hypertension in the number one position because of the need for frequent visits and stabilization of the blood pressure.

It is apparent that the ICHPPC utilizes not only diagnoses, but also symptoms. Thus, the physician can code visits as he sees them. If the physician cannot justify pneumonia, he can code for cough in the classification. Later as the physician follows his patient, the code can be changed to pneumonia, bronchogenic carcinoma, etc. if the workup so indicates.

Some of the uses of the diagnostic index can be in the enumeration of high incidence encounters in primary care. Thus, the curriculum of the Residency Program can be planned to cover all of these subjects during a set period of time. Consultants in specialty fields visit our program and easily audit charts of patients with a given diagnosis.⁷ A physician who wishes to discontinue oral diabetic agents,

*Assistant Director, Family Medicine Institute.

†Inquiries may be directed to the office of the American Hospital Association, 840 North Lakeshore Drive, Chicago, Illinois, 60611.

TABLE 1

AGE-SEX ANALYSIS OF THE FAMILY MEDICINE
INSTITUTE'S PATIENTS AS OF JUNE, 1975

Age in Years	Male	Female	Total
0-4	107	97	204
5-9	104	87	191
10-14	85	91	176
15-24	289	601	890
25-34	398	533	931
35-44	144	220	364
45-54	120	197	317
55-64	98	146	244
65+	101	171	272
TOTAL PATIENTS	1,446	2,143	3,589

may easily do this by having the charts pulled on his diabetic patients. In outreach, the diagnostic index would allow the health care team to notify those cohorts of patients in high risk groups to come in for influenza injections. Overall, the index would give the physician a better understanding of his practice. He could accordingly plan his postgraduate courses to include more of the common problems encountered in his practice. A more far reaching use would be in PSRO activities. The audit of hospital charts for quality of care has become standard practice throughout the State. In the not too distant future, this practice may extend to primary care facilities.

In summary, an analysis of our practice over a fourteen-month period has been presented. In addition, methods of data retrieval and their practical use in a busy primary care practice are elucidated.

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TABLE 2

FAMILY MEDICINE INSTITUTE
THIRTY MOST COMMON REASONS FOR VISIT

Code	Disease	Total Visits
401	Ess. Benign Hypertension	665
460	Upper Respiratory Tract Inf.	535
901	Gen. Med. Exam. (req. by agency)	380
900	General Medical Exam	287
903	Pap	281
277	Obesity	228
304	Depressive Neurosis	195
921	Oral Contraceptive	189
595	Cystitis & Urinary Infec.	184
250	Diabetes Mellitus	174
381	Acute Otitis Media	160
905	Prophylactic Inoculation & Vac.	153
300	Anxiety Neurosis	137
772	Abdominal pain inc. infant colic	137
412	Chronic Ischemic H.D.	108
322	Abuse of Tobacco	103
278	Dis. of Lipid Metabolism	96
614	Vaginitis	96
718	Low Back Pain	96
691	Eczema & Dermatitis	93
870	Laceration, Open Wound	83
944	Neonatal care & rout. exam of children	77
466	Acute Bronchitis	76
680	Boil & Carbuncle	74
315	Transient sit. Disturbances	70
937	Prenatal Care	70
750	Chest Pain	61
713	Osteoarthritis	57
461	Sinusitis	55
716	Shoulder Syndromes	51

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Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The bylaws of the Maine Medical Association were amended in June of 1973 as follows: Chapter I, Section 11, — "Each member of the Maine Medical Association shall be required to report his activities in continuing medical education every year according to a format provided by the Committee on Continuing Medical Education."

Only active, dues-paying members are required to report this year.

Please fill in your activity report promptly and return to the M.M.A. office, P.O. Box 250, Brunswick, Maine 04011.

Congenital Dysplasia of the Hip in the Newborn — A Second Look

ROBERT B. DAY, M.D.

Physicians responsible for the examination of newborn infants have become increasingly aware of congenital dysplasia of the hip (CDH). Now, almost universally, infants are carefully checked for this condition. This increased awareness in the medical community has made possible the early diagnosis and treatment of CDH. Despite this increased awareness, certain misconceptions have allowed the occasional infant with CDH to go unrecognized. It will be the purpose of this article to point out these misconceptions in the hope that better understanding of the disease process and diagnostic tests will allow for further improvement in our diagnostic accuracy.

It would be well to define certain terms that will be used repeatedly. Congenital dysplasia is a congenital maldevelopment of the hip joint, including abnormalities in the proximal femur, the acetabulum, and the ligamentous structures about the hip. It may be considered a precursor of congenital subluxation and dislocation. In subluxation the cartilage of the femoral head and acetabulum are in contact, but in an abnormal relationship, whereas in dislocation, the femoral head is entirely out of the acetabulum and the cartilage is not in contact.

The natural history of a dysplastic hip is variable (see diagram 1). Both environmental and hereditary factors influence the subsequent course. Subluxation or dislocation may occur during the first year of life, or a dysplastic hip may simply remain dysplastic and go unrecognized until premature degenerative arthritis occurs in adult life. Also, some dysplastic hips become normal even without treatment; if the femoral head remains in a normal relationship with the acetabulum, the acetabulum may develop normally.

It is rare for a hip to be subluxed or dislocated at birth. The rare intrauterine dislocation is classified as "teratologic" because there are often associated congenital anomalies and the response to treatment is quite different from the typical hip dislocation. The physical signs in these teratologic hips are obvious and rarely overlooked. On the other hand, typical congenital dislocation is a postnatal phenomena, usually occurring in the first year of life. In the newborn the hip is dysplastic and *not* dislocated. If this important fact were remembered, there would be much less confusion in the examination of the newborn.

The classical findings of asymmetric skin creases,

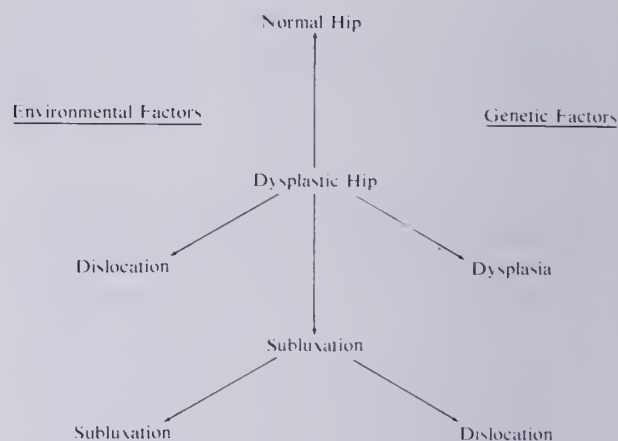


Diagram 1

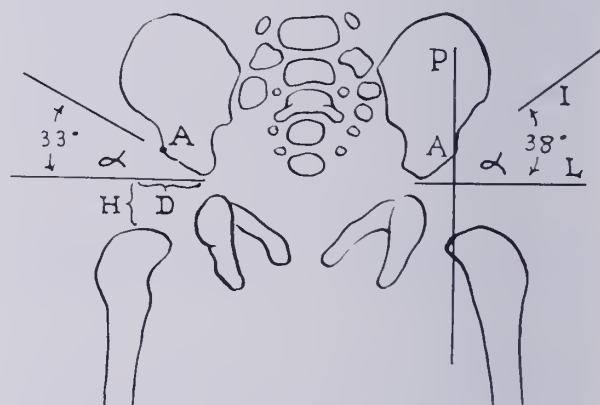


Diagram 2

Drawing from roentgenogram of the pelvis of a newborn infant. (This infant's hips were normal on physical examination.) *A* indicates the anterior inferior iliac spine; *L* is horizontal line of Hilgenreiner, drawn through comparable points on the triradiate cartilage; *I* is line drawn parallel to acetabular roof—angle formed between *I* and *L* is acetabular index (*a*); *P* is Perkins's line, a perpendicular dropped through the anterior inferior iliac spine at right angles to *L*; *H* is the distance between *L* and the highest point on the femoral neck; and *D* is the distance between the triradiate cartilage and the intersection of *H* and *L*. (Reproduced from *Diagnosis of Congenital Dysplasia of the Hip in the Newborn Infant* by S. S. Coleman. *Journal of the American Medical Association*, 162: 550, 1956.)

adduction contracture, unilateral shortening, and the Ortolani sign are absent in the newborn with CDH. Asymmetric skin creases and unilateral shortening only occur in established subluxation or dislocation, and depend on the shortening that oc-



Fig. 1. Bilateral congenital hip dislocation undetected until 2 years of age.



Figs. 2 and 3. Newborn American Indian infant had careful clinical examination and x-ray because of strong family history of CDH. Both were felt to be normal. The child was lost to follow up until age five when dislocation was discovered.

curs when the femoral head lies posterior and superior to the acetabulum. Slight asymmetry of the skin creases can occur in normal infants with physiologic hip flexion contractures secondary to intra-uterine position; however, definite shortening and prominent asymmetry are late findings present in established dislocations or subluxation only.

Inability to completely abduct the flexed hip, i.e., an adduction contracture, is also rarely present in the newborn. This is explained by the fact that the contracture is not a true contracture at all, but simply a relative lengthening of the adductor muscle mass secondary to lateral displacement of the femoral head in subluxation or dislocation.⁴

Probably the least understood diagnostic test is the Ortolani test or "click test." Much misunderstanding stems from the fact that ligamentous clicks are a normal and not uncommon phenomenon and must not be confused with the "click of entry" of the dislocated femoral head into the acetabulum as described by Ortolani. Because the femoral head is

almost always in the acetabulum, the click of entry cannot be elicited. In a dysplastic hip with a deficient acetabulum, ligament laxity, or both, it is possible to gently dislocate the femoral head posteriorly and superiorly with gentle pressure.^{1,3} One must be extremely patient, however, and have a relaxed infant that is not struggling in order to successfully elicit this subtle sign. This is the most important diagnostic test in the clinical examination. The technique is simple once learned. The infant is placed on his back with the hips flexed 90° and the knees also fully flexed. The examining hand encircles the thigh and calf with the index and middle fingers palpating the greater trochanter and the thumb resting over the femoral triangle. Then with gentle superior and lateral pressure from the thumb and hand the femoral head may be felt to ride over the posterior acetabular rim. I would emphasize that this is *not* a

distinct palpable and audible click, but rather a subtle but definite feeling of the dislocation.

X-rays are frequently ordered when there are suspicious findings on clinical examinations. One must be alert to the fact that a "normal x-ray" does not rule out the presence of hip dysplasia. In the newborn the proximal femur and the pelvis are primarily cartilaginous. Only the ossification centers are visible radiographically. Consequently, the detailed bony anatomy is impossible to establish. Classically the "acetabular index" has been used as a measure of hip development. This represents the slope of the roof of the acetabulum (see diagram 2). The problem is that there is a wide range of normal values; 30° has been the accepted figure, but one authority feels that only those hips greater than 40° can be considered abnormal,³ and another has recommended abandoning the use of acetabular index entirely in the early diagnosis of congenital dysplasia.² In referring to the figure below, if the medial and proximal portion of the femoral metaphysis lies lateral to

the vertical line "P" then this is diagnostic of dysplasia. One study found this to be the most important x-ray findings in the series but it was present in only 50% of clinically dysplastic hips.³ Therefore, it is important to remember that in the newborn, congenital hip dysplasia is not an x-ray diagnosis.

In summary, one cannot depend on a negative x-ray examination or on the absence of the classical physical findings in ruling out congenital dysplasia of the hip in the newborn. Even the experienced examiner can easily miss the subtle displacement of the femoral head on physical examination. Therefore, repeat examinations should be done during the first year of life on all infants as part of their "well baby" care.

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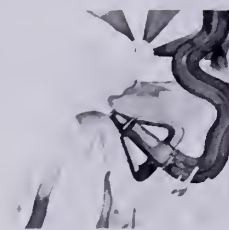
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* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium fre-

quently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy

patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

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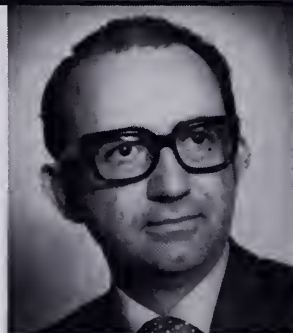
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Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complication or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

main purpose of drug information for the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with this agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a long one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebotrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005



A Geriatric Program in Sanford, Maine

MELVIN BACON, M.D., F.A.G.S.*

For many years I have been interested in the care of the elderly. Last year was no exception. This interest dates back many years to when my truly wonderful mother's parents were living. Their continued interest, encouragement and consideration stirred me on. Even while I was growing up, they encouraged me to aid and assist the elderly whenever possible reminding me that one day, "The Good Lord Willing," I would fall into this category. With such a background as I have already mentioned, this interest has continued up to the present and has prompted me to write this paper on the Geriatric Program in Sanford. It is believed that there are only 2 such programs in the United States.

I should like to start by describing the Trafton Senior Citizen Center which has been one of my main interests, giving a little of the background and history and its programs.

The Center was started in 1964 under the auspices of the Sanford-Springvale Y.M.C.A. under the supervision of Thomas Milligan, Executive Director, and has had four locations. It has grown steadily in scope. On May 4, 1969, a realization came to pass with the dedication of the Charles A. Trafton Memorial Senior Citizen Center in Sanford. They now have their own building. This came to pass through the generosity of Mr. and Mrs. Emile Levasseur. It is for citizens age 50 and over.

Many activities have been going on there. The following, of interest, is the Well-Aging Clinic Program from September 26, 1973 to August 28, 1974. The Clinic Program is as follows:

1973

SEPTEMBER

Wednesday 26 Blood Pressure
1:30 P.M.
Wednesday 26 Fall Bus Trip

OCTOBER

Thursday 18 Foot Care
1:30 P.M.
Wednesday 24 Influenza Vaccine
Wednesday 24 Blood Pressure
1:30 P.M.
Wednesday 31 Hearing Evaluation
1:30 P.M.

NOVEMBER

Wednesday 7 Influenza Vaccine

*Medical Advisor to the Charles A. Trafton Senior Citizen Center, Chief of Medicine and Director of Medical Education, Goodall Hospital, Sanford, Maine.

Tuesday 13 Diabetes Program (Talk)
Thursday 15 Blood Sugar Testing
Wednesday 28 Blood Pressure
1:30 P.M.

DECEMBER

Thursday 6 Glaucoma Clinic
1:30 P.M.
Wednesday 26 Blood Pressure
1:30 P.M.

1974

JANUARY

Wednesday 16 Foot Care
1:30 P.M.
Wednesday 23 Blood Pressure
1:30 P.M.
Wednesday 30 Hearing Evaluation
1:30 P.M.

FEBRUARY

Tuesday 7 Bus Trip
Tuesday 13 Heart Program (Talk)
Wednesday 27 Blood Pressure
1:30 P.M.

MARCH

Wednesday 27 Blood Pressure
1:30 P.M.

APRIL

Wednesday 10 Foot Care
1:30 P.M.
Wednesday 24 Blood Pressure
1:30 P.M.

MAY

Wednesday 22 Blood Pressure
1:30 P.M.
Wednesday 29 Hearing Evaluation
1:30 P.M.

JUNE

Wednesday 26 Blood Pressure
1:30 P.M.

JULY

Wednesday 10 Foot Care
1:30 P.M.
Wednesday 24 Blood Pressure
1:30 P.M.
Wednesday 31 Hearing Evaluation
1:30 P.M.

AUGUST

Wednesday 28 Blood Pressure
1:30 P.M.

It appears appropriate at this time to give the results of this program. The period for these results is from March 1973 to March 1974.

The number of blood pressures taken was 511 and the number of abnormals found was 95, and each was referred to the family physician for study and treatment. There were 247 Influenza injections given. Twenty-five audiometric tests were done of which 12 were found to be abnormal and referred to the family physician. Eight cases of foot care were done and none were referred. Sixteen individuals were checked for Glaucoma and 2 cases were referred to the family physician. One of these was found to have Glaucoma and the other was found to be borderline. Another interesting finding was that of the blood sugar testing program. Fifty-seven were done and 5 were found to be abnormal. Of these, 4 were found to be new diabetics and one a known diabetic.

The next item concerns the bus trips. Forty-nine took the Songo River Boat Cruise in Naples, Maine, and 90 attended the Ice Follies at the Boston Gardens, Boston, Massachusetts. It was interesting to note the enthusiasm of the participants in this endeavor. It should be mentioned at this time that a nurse accompanies all bus trips.

The purpose of the "Well-Aging Clinic" is to provide a health service for the Senior Citizens of the area, who, for many reasons, might not otherwise be able to obtain these services.

The Community Health Association, having an interest in the senior citizens of the area, accepted the challenge of trying to provide, at the lowest possible cost, a series of test immunization and medical programs, which could determine if further medical services were needed by each individual's physician. The program has the acceptance of most of the local physicians.

A multiplicity of literature including information bulletins is available at the Center.

Speakers on various health and safety subjects have also participated.

Another program of interest was a hot lunch program sponsored by the Cumberland-York County Senior Citizens Council five days a week. It is presently federally funded and there is no charge. However, people are asked to donate whatever they wish or \$1.00 if possible. Similar programs are being carried out in Biddeford, Westbrook and Portland.

There was also a physical fitness program on Mondays, 10:00 A.M. to 11:00 A.M. for all senior citizens age 50 and over. The Director of this program was Mrs. Eva Spencer.

Other endeavors included social and fun activities, hobby shows, food sales, painting classes,

beano games, whist parties, trash and treasure sales, the Annual Fair to raise funds for operational expenses and a variety of speakers.

Another interesting feature was referral, assisting and counseling regarding Maine's Elderly Householders Tax Relief and Federal Income Tax assistance given by Mr. Raymond Chevalier.

The Center also has a column in the Sanford Tribune which indicates activities that go on at the Center. They also have a bulletin board at the Center for the information of the senior citizens.

Now to include a few other ideas. We had arranged for speakers on Blue Cross/Blue Shield Companion Plan for individuals age 65 and over and on the Medicare Program to speak before this group last fall.

Another endeavor for any citizens age 50 and over was planned. It would involve the Sanford-Springvale Community Health Association and the Traf-ton Senior Citizens Center in Sanford. The facilities of the latter group would be utilized. This set-up would include doing ECGs, CBCs, SMA 12s, Lipid Profiles, Chest X-rays, Pulmonary Function Tests and Urinalysis. Blood Pressures would also be taken and each individual weighed and measured. A short pertinent history would be taken by a nurse or completed by the participant. About 300 individuals would be examined. This program would be open to all from Sanford, Springvale, Acton and Shapleigh. Although several groups were approached to subsidize this program, we were turned down by all. We have as yet not found the "Key to Success" in this area. However, if all goes as anticipated, we will be setting up a screening program much smaller and different in scope that should prove most interesting. This will include complete histories simplified enough to be filled out by the senior citizen himself, and a very thorough and adequate physical examination will be performed. The history will be reviewed by the participating physician. In addition, "Pap Smears" will be done on all females. Urinalysis and Hemoglobins will be done on all. All those found to have abnormalities will be referred to the family physician.

NURSING PROGRAMS

Also interesting was a series of Workshops for the nurses of Maine which, in part or whole, involves the Geriatric Program. These had the approval of the Maine Medical Association and the York County Medical Society. There was an attendance of from 150 to 200. The subjects of these were stroke, diabetes and geriatrics.

SUMMARY

This paper presents the Geriatric Program in Sanford. We believe we have been pioneers in this field.

Continued on Page 217

President's Address*

JOHN B. MADIGAN, M.D.

This evening, as the time has come for my Swan Song as President of the Maine Medical Association, I wish to state first of all my gratitude for the confidence in me expressed by those who elected me to office and for the privilege of serving. I trust that confidence has not been misplaced. Secondly, my thanks flow in profusion to the base of operations of the Medical Association, namely, Patti Bergeron, the staff and, of course Dan Hanley, without whom the Association would be as a ship without a rudder. The Executive Committee also has been most cooperative and supportive of my efforts.

It has been a busy and exciting year! You are all aware of the many disturbing changes affecting the practice of medicine in our times. In my travels to the various Districts of the State, I have stressed my concerns relevant to the problems of the profession. I have been encouraged to find an increasing number of physicians interested in becoming more active in committee work and in the general business of the Association. No doubt the difficulties we face have contributed to this interest but if these are the stimuli, at least interest in the Association has been aroused.

In this day and age the best efforts of conscientious physicians to provide medical care for the individual who is sick are now constantly diluted and frustrated by rules and regulations of third party payers both governmental and in the private sector. The judgement of physicians to decide who needs hospital care and then to regulate the length of stay is now in question. The treatment of disease becomes the paramount issue and the care of the sick is of secondary significance. In such ways, the interrelationships between physicians and patients are gradually eroded, contributing to declining confidence in the doctor and the eventual environment for liability procedures.

Such an environment unquestionably is also due to changes in life styles and attitudes of people all over the world. There is a growing tendency to trust no one and rather to be suspicious of any indication of sincerity. It is a time of terrible turmoil for physicians!

Faced with such a situation, let us reflect for a moment on a few fundamental truths which we once held close to our hearts and let us question whether if we once held to these ideals should we not now rethink our philosophies when overwhelmed with

problems such as are currently on the medical horizon.

The history of medicine is a necessary framework to integrate all the numerous fragments of medical theory and practice. It teaches us that medicine is so complex that no human mind can absorb it all. The doctor, of necessity, must be a wise man in order to be able to sort out and apply this complex knowledge. It follows, he must be a good man because how else can he combine professional quality and integrity with a kind heart, high ideals, and perform with honesty and efficiency as a member of society.

Thus, the physician in his threefold capacity as a professional, as a member of society, and as a human being has helped man in his physical, mental, and social ascent throughout the ages. Hence, to be a doctor is much more than dispensing pills, patching or repairing torn flesh or minds. Indeed, it is more than Utilization Reviews, Peer Reviews, and multiple insurance forms. It is a profession which should have the highest potential for greatness. Think of our famous colleagues throughout history who have contributed in dynamic ways to the science and art of medicine. Our profession is the only one which still speaks of its duties to mankind while others speak only of rights. We are dedicated in service to our patients, but perhaps in this cynical world this is hardly a conceivable attitude. As clinicians, we must alleviate pain and heal the sick and as teachers we must spread our knowledge for the benefit of mankind with no ambition for gain. In this way, we shall maintain our profession as a social science applied to the welfare of mankind. In a very personal sense, it is important for each of us to treat our patients with kindness, courtesy, and honesty — striving to preserve our own modesty and humility — maintaining always the greatest personal simplicity.

Hopefully our own patients can sense an approach to these qualities in each of us. Unfortunately at present, it is politically expedient to have professional health planners ignore any such qualities in the medical community and to portray us as a mercenary band of elite money grabbers completely unsympathetic to the poor and unfortunate, repeated denials of such designations can do very little to correct the image inferred by such modern day planners. The only defense can be our continued efforts to live up to the highest standards in the care of the sick and unfortunate of this world.

Continued on Page 220

*Presented at the 1975 annual session of the Maine Medical Association.



Maine Blue Cross and Blue Shield News

UPDATE ON OUTPATIENT BENEFITS

Executive Committee members of the Maine Blue Cross and Blue Shield Board have approved recommendations dealing with the 1974 expansion of the Blue Cross outpatient laboratory coverage and any future growth of a Blue Shield plan for outpatient laboratory services.

Maine Blue Cross and Blue Shield representatives, working closely with an ad hoc committee of physicians and hospital officials, studied proposals concerning the Blue Cross Pilot Outpatient Laboratory Program. After a great deal of study and deliberation, they brought their recommendations before the executive committee.

Last year, Maine Blue Cross instituted, on a pilot basis, coverage for hospital outpatient laboratory testing and pathology utilized in diagnosing injury and disease.

Many physicians voiced concern over the expansion, feeling that it would cause an inconvenience to both physicians with small office labs and their patients, arising from the need to refer the patient to the hospital outpatient department in order to have the lab work covered by Maine Blue Cross and Blue Shield.

Feedback from physicians also indicated that they would like to be able to take specimens in their offices and send them to the nearest hospital and have the patient still receive coverage. Thus, the cooperative study came into being in response to physician concern.

The Executive Committee further accepted these recommendations:

- * The equalization of Blue Cross and Blue Shield coverage will be accorded top priority, if at some time in the future, Blue Shield achieves a financial and competitive position which would permit such expansion of its coverage.
- * Enlargement of the current pilot program to include payment for processing of samples obtained in the physicians' office and transported to the hospital laboratory. The hospital also would be reimbursed according to the current reimbursement formula for cost of the necessary laboratory materials.
- * Physicians should not feel restricted in billing patients, who are Blue Cross members, for sample drawings which take place in their offices and are processed in hospital laboratories.

Presently, in addition to the Blue Cross pilot program, Blue Shield has a rider which provides office laboratory coverage. A special notation can be found on the I.D. cards of subscribers in groups that have purchased this optional rider.



DEAN H. FISHER, M.D.
COMMISSIONER

State of Maine

Department of Health and Welfare

Gonorrhea in Maine

CHARLES LINDMAN*

The incidence of gonorrhea in Maine for 1974 reached an all-time high with 2,080 cases reported to the Bureau of Health. This total represents a 53% increase over 1,379 cases reported for 1973. The implementation of specific control measures in early 1972 has contributed significantly to the continuous rise in reported gonorrhea cases. Specifically, these measures to control gonorrhea in Maine include a Statewide gonorrhea culture screening program, a required laboratory venereal disease reporting system and the epidemiological management of male cases of gonorrhea. It appears that the combination of these activities may be able to effect some control over gonorrhea, provided continued support for control efforts will be forthcoming.

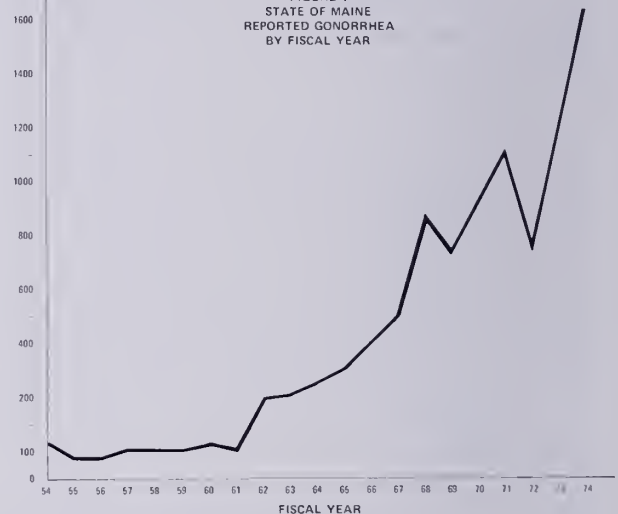
The Problem

1. Time — Figure 1 shows the number of cases reported in Maine from 1954 through 1974. The curve is similar to that seen nationwide and represents a significant rise in the incidence of gonorrhea which has been most marked in the past five years. An all-time peak of 2,080 cases reported in calendar year 1974 represents a 53% increase over 1973. It is of some interest that the incidence of gonorrhea declined in both New Hampshire and Vermont during 1974. Maine presently ranks third in New England based on a rate per 100,000 population. Only Connecticut and Massachusetts reported more cases than Maine. Nationally, in 1974, Maine ranked 38th among the states, based on a 100,000 population rate, which is probably consistent with other reportable communicable disease rates.

2. Place — Figure 2 shows the reported incidence rates of gonorrhea by county for Maine in 1974. The counties with the highest incidence rates are Cumberland, Penobscot, Kennebec and Androscoggin, locations of the four largest cities in Maine (Portland, Bangor, Augusta/Waterville and Lewiston/Auburn, respectively). The counties with the lowest incidence tend to be those which are rural.

*Director, V.D. Control Program, Bureau of Health

FIGURE 1
STATE OF MAINE
REPORTED GONORRHEA
BY FISCAL YEAR



Considering further the distribution of gonorrhea within Maine, Table 1 shows the reported 1974 incidence of gonorrhea in counties belonging to Standard Metropolitan Statistical Areas. Within SMSA counties, the incidence rate within large cities (central cities) is compared with places outside SMSAs. A very clear comparison between incidence in more dispersed areas and densely populated areas is seen, with the central cities reporting the much higher incidence of gonorrhea. This difference reflects a variety of factors including greater availability of medical care facilities, plus the existence of the social and environmental conditions that historically contribute to the spread of venereal disease.

3. Person — Figure 3 shows age specific groupings for males and for females, comparing 1965 and 1974. It is obvious that the same age groups are affected now as were affected 9 years ago, with the highest incidence seen in 20 to 24 year olds. About 75% of the cases occur in those under the age of 25. The male to female ratio, which was 1:0.6 in 1965, has increased to 1:1.1 in 1974, suggesting that previously undiscovered females are presently

FIGURE 2
STATE OF MAINE
GONORRHEA RATE PER 10,000 POP
BY COUNTY - 1974

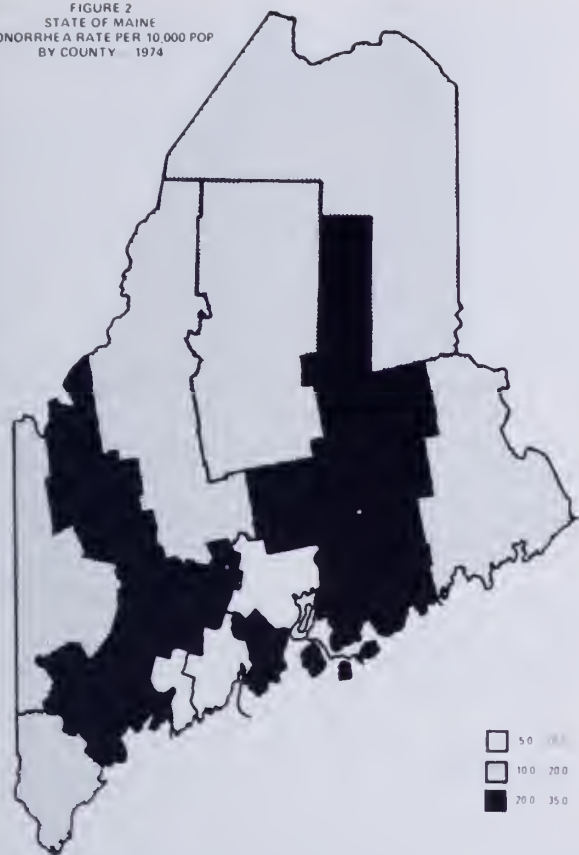
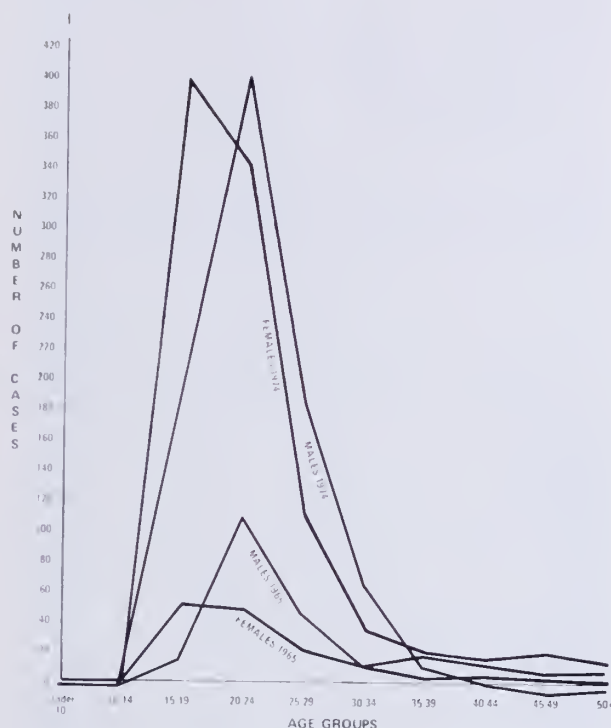


FIGURE 3
STATE OF MAINE
GONORRHEA CASES
BY AGE GROUPS - COMPARING 1965 & 1974



being detected. The increase of reported cases in the 15 to 19 age group undoubtedly was influenced by a 1970 legislative mandate allowing physicians to treat minors without first obtaining parental permission.

Table 2 shows a comparison between the total infected population and the at-risk age group (between 15 and 29) based on incidence rates per 10,000 for 1974, by county breakdown. The incidence levels in the 15 to 29 group clearly illustrates the fact that gonorrhea is most common among the teenage and young adult groups more than any age group. Of the 2,080 cases reported in 1974, 1,427 (78%) occurred within the 15 to 29 age group. When observed by itself, the case rate per 10,000 population in the 15 to 29 age group is nearly 5 times greater than the rate for the total population in each county. Considering the yield factors by age groups, it is recommended that only females under 30 years of age be routinely examined for gonorrhea.

The Program

1. Casefinding — In April 1972, a Statewide gonorrhea screening program was initiated by the Bureau of Health. Transgrow medium was furnished to any health care provider, and free processing support was offered by the State Public Health Laboratory in Augusta. The program has been well

received by many components of the medical care system throughout Maine. Since April of 1972, 45,769 females have been examined for gonorrhea by a variety of health care providers. The thrust of this mass screening effort has been directed at the 15 to 40 age group. The overall positive rate for 1974 was 3.4%, with the greatest yield again occurring in the 15 to 29 age group.

Table 3 shows the results of screening cultures according to the type of facility submitting the culture. As might be expected, cultures taken in the State's only designated venereal disease clinic had the highest positive rate (22%). Family planning facilities, which accounted for 43% of all cultures submitted, had an overall positive rate of 2% and private physicians who submitted 43% of all cultures had a positive rate of 3%. Positive rates in Maine's screening program are much lower than those reported from the nation as a whole. The value of family planning screening can be assessed in one word, "routine." Since the inception of the screening activity, family planning programs throughout the State have presented the most convenient and inexpensive medical setting through which young people can be examined for gonorrhea on a routine and confidential basis.

2. Treatment — Since there is only one full time V.D. clinic in Maine, most of the cases of gonorrhea

TABLE 1

STATE OF MAINE GONORRHEA CASES PER 100,000 BY TYPE OF AREA

Area	Rate/100,000
Total State	208.0
Metropolitan (inside SMSAs total)	414.9
Central Cities (Portland & Lewiston)	552.2
Non-Metropolitan (outside SMSAs total)	114.5

TABLE 2

STATE OF MAINE REPORTED GONORRHEA CASE RATE/10,000
ALL AGES VS. AT-RISK GROUP (19-29) BY COUNTY
CALENDAR YEAR 1974

County	Total Cases Reported	Total Rate All Ages	Rate Based on Pop. for 19-29 Group
Androscoggin	220	24.1	107.8
Aroostook	111	11.7	50.3
Cumberland	668	34.6	149.2
Franklin	54	24.0	99.0
Hancock	70	20.2	95.6
Kennebec	232	24.3	110.0
Knox	66	22.7	113.6
Lincoln	13	6.3	33.8
Oxford	57	13.1	65.4
Penobscot	311	24.8	92.6
Piscataquis	12	7.3	36.3
Sagadahoc	14	5.9	27.2
Somerset	38	9.3	45.0
Waldo	15	6.4	29.1
Washington	53	17.7	90.0
York	146	13.3	56.0

are seen and treated in private physician offices, hospital based out-patient clinics and emergency rooms. In rural areas it has not been feasible nor economically possible to establish formal V.D. clinics due to dispersion of the population. In these areas, arrangements have periodically been made with private physicians, hospital emergency rooms, etc. to provide examination and treatment for persons suspected of having a venereal disease. The Bureau of Health presently supplies aqueous procaine penicillin, ampicillin and spectinomycin free of charge to physicians, family planning clinics and local health departments for use in treating venereal disease patients. To insure physician awareness of the new recommended treatment schedules for gonorrhea, the schedules are published periodically in the appropriate state and national medical literature. The latest treatment schedule recently appeared in the January 1975 edition of the Maine Medical Journal.

The Bureau of Health's casefinding capability was enhanced in 1974 by the implementation of a Statewide laboratory reporting regulation which requires all positive diagnostic tests for venereal disease to be reported directly to the Bureau's Venereal Disease Control Program in Augusta. The in-

TABLE 3

STATE OF MAINE GONORRHEA SCREENING
POSITIVITY RATE OF FEMALES EXAMINED ACCORDING TO
TYPE OF FACILITY

Submitting Facility	Positive/Total	% Positive
Private Physicians	359/11,516	3.1
Family Planning Clinics	230/11,316	2.1
V.D. Clinic	131/589	22.2
Hospital Outpatient	116/907	12.8
Group Health Clinics	24/473	5.1
Student Health Centers	18/785	2.3
Correction Center	6/168	3.6
Hospital Inpatient	5/252	2.0
Military	0/55	0
Not Specified	7/88	8.0
TOTAL	896/26,149	3.4

TABLE 4

STATE OF MAINE REPORTED MALE GONORRHEA CASES ONLY
EPIDEMIOLOGIC YIELD FOR 1974

	Private Cases No.	Cases %	Public Cases No.	Cases %
Male Cases Reported	832		190	
Cases Interviewed	318	38.2	182	95.8
Total Contacts Examined	418		258	
Contacts Infected with GC	127	30.4	77	29.8
Contacts Epidemiologically Rx	99	23.7	70	27.1
Total Treatments	226	54.1	147	57.0

tent of this surveillance mechanism is to facilitate and hasten the epidemiological process thereby extending a more comprehensive and productive service to the private medical community throughout Maine. Realizing the need to maintain the confidential relationship between the physician and his patient, under no circumstances will venereal disease control personnel ever contact a patient without first obtaining the reporting physician's advice and permission to do so.

3. Case Evaluation — A selective program on gonorrhea casefinding was initiated in October 1972. Infected male gonorrhea patients have been interviewed for their sex partners. The main focus of this epidemiological activity has been centered in the larger cities of the State. Table 4 shows the results of gonorrhea case evaluations in 1974.

Overall, 38% of the male gonorrhea patients referred by private physicians and 96% of the male patients seen in public facilities were interviewed in 1974. Less than 5% of the total female gonorrhea patients reported in 1974 were interviewed by program personnel. The average number of contacts from male gonorrhea patients was 1.50. Persons infected with gonorrhea are motivated to identify all sexual contacts within a 30-day period prior to receiving treatment. Of contact investigations assigned, over 75% resulted in the examination of patients. Of those examined, 30% of all female contacts to male patients were diagnosed as having

gonorrhea. Three-fourths of these were either asymptomatic or previously untreated. An additional 25% were given preventive treatment, reflecting an overall total of 55% of examined contacts receiving treatment.

Physicians, in general, throughout Maine have become more aware of the venereal disease situation in their communities and have consequently participated in the control effort through better reporting practices and requests for control services. Unlike infectious syphilis, gonorrhea presents an entirely different disease problem to apply standard control measures. The short incubation period and the large number of reported cases of gonorrhea makes the "face-to-face" method of control difficult to accomplish. Geography and limited manpower and resources in Maine make it virtually impossible to reach an adequate number of the infected population whereby an interruption in the spread of disease can be expected. However, if epidemiological interceptors are applied to enough cases, the random spread of gonorrhea could be interrupted and eventually stabilized. The situation requires an alternate and perhaps a more effective approach to casefinding.

To further advance this renewed spirit of cooperation, physicians located in high-incidence areas of the State will be asked to participate in a new approach to the epidemiological control of gonorrhea. The chief features of this new approach to casefinding include the following:

1. Responsibility of contact referral is shared

equally by the treating physician and his patient.

2. Distribution of a patient motivational kit which will contain a brief description of the symptoms and effects of gonorrhea. The kit will contain two referral packets to be given to the last two sex contacts of the infected patient. The physician will be asked to give the patient a few brief statements about the infection and instruct the patient to give these kits to his contacts.

3. Serve to diminish some of the traditional apprehensions both physicians and venereal disease patients have expressed regarding "confidentiality" and the need to report to the public health authority.

4. Extend to the physician a "positive" option whereby he can utilize the control services of public health when he feels the situation may require it (e.g. patient doesn't want to approach his contacts, geographical problems, etc.)

The objective of this physician orientated casefinding activity will be to place the responsibility of contact referral on the infected patient. Initially, a select number of physicians will be asked to participate in the endeavor in order to initially measure its impact as a productive casefinding method.

Since 75% of all cases of gonorrhea are reported by private physicians in Maine, any degree of control hinges on a mutual and cooperative effort by the public and private sector. It is to that end, the Bureau of Health will direct its venereal disease control resources.

A GERIATRIC PROGRAM IN SANFORD, MAINE — *Continued from Page 211*

Credit for the success of this program should be given to the tireless efforts of the volunteer Hosts and Hostesses, the Program and Project Committee, the Rhythm Band, the Community Health Association staff under the leadership of Marolyn Roberts, R.N., Director of Nursing, the officers and directors of the Sanford-Springvale Y.M.C.A. and its staff. In closing, may I again single out Thomas Milligan, Executive Director of the Y.M.C.A., for his tireless efforts in this endeavor.

He has been an inspiration and a bulwark of support. I also must mention the generosity of Mr. and Mrs. Emile Levasseur, who through their help made the Trafton Senior Citizen Center, in memory of Charles A. Trafton, a reality. May I add this dictum, "If you live a life of usefulness trying always to help others, you need not seek happiness . . . it will come with each rising sun." This certainly pertains to all the participants in this endeavor.

News, Notes and Announcements

Summer Programs at Colby College, 1975
The 30th Annual Lancaster Course in Ophthalmology
June 14 to August 22

7th Seminar in Nuclear Medicine
August 18 to 22

2nd Seminar in Pulmonary Disease
August 24 to 28

2nd Seminar in Forensic Medicine
August 24 to 27

A Screening Program for Senior Citizens in Sanford

For many years I have been interested in the elderly. For many years I have tried to get funds to carry on a screening program for the Senior Citizens (age 65 and over) in Sanford. This was to no avail for I was always told there were no funds available for this despite the number of organizations who state they are interested in the welfare of this group.

However, through continued efforts of myself, Thomas Milligan, Executive Director of the Sanford-Springvale YMCA and the Trafton Senior Citizen Center, and Mrs. Marolyn Roberts, Director of Nurses of the Sanford-Springvale Community Health Association, this program became a realization on December 7, 1974. The facilities of the Trafton Senior Citizens Center were utilized. Two rooms were set up so simultaneous exams could be carried on by two physicians. Each of us was assisted by a nurse.

Now to turn to the format of this program. A history form was given to each participant to complete. It included name, birth date, and name of personal physician. It also had a series of questions including symptoms, hospitalizations, previous illnesses, and surgery. It was very comprehensive and easy to complete. This was to be completed prior to the date of the examination.

Each patient had weight, height, temperature, blood pressure and pulse taken. In addition their hemoglobin and urine were checked. I examined the head, ears, eyes, nose, mouth, throat, chest, lungs, heart, bones and joints, skin, glands, extremities and also did a neurological exam. My associate examined the breasts, abdomen, and did vaginal, rectal and pap smear on the women. On the males, he examined the abdomen, did a rectal, checked for hernias, and their genitalia.

I should mention at this time that each nurse brought to our attention at the time of each exam, pertinent information indicated on the form completed prior to this examination. She also informed us of any problem with the vital signs, hemoglobin and urinalysis.

We have had three clinics thus far. I am truly amazed at the amount of pathology discovered. It is my feeling that there is a great need for preventive medicine.

I certainly was pleased to be a part of this program and it appears to be of interest and importance to present it to you.

MELVIN BACON, M.D.

Fellow of American Geriatric Society
Sanford, Maine 04073

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County Society Notes

York

The March meeting of the York County Medical Society was held at the Goodall Hospital, Sanford, Maine on March 12, 1975.

The format of the meeting consisted of a Social Hour from 6:30 p.m. to 7:30 p.m., Dinner at 7:30 p.m. with the speaker and business meeting following.

The meeting was presided over by Dr. Carl E. Richards, Sanford, President of the Society.

The featured speaker of the evening was Martin F. Ulan, Administrator, York Hospital, York, Maine. His subject was "Federal and State Legislation Concerning Physicians and Hospitals to Include PSRO, Newer Developments, Status of Southern Maine Comprehensive Health Association."

The talk was most informative and a lively discussion followed. The minutes of the previous meeting were dispensed with.

Mr. Peter Booth, the new administrator of the Goodall Hospital, was introduced. James H. Swarr, M.D., A.P.L., Ophthalmologist, was unanimously voted into membership in the Society.

The following resolution: "Whereas physicians often find it difficult to keep themselves informed about legislative matters: Therefore, be it resolved that the Maine Medical Association issue a legislative newsletter at appropriate intervals to keep its members informed of State or Federal legislation that may affect the practice of medicine in this State," was presented by Dr. Leopold A. Viger, to be presented to the next House of Delegates and was so voted.

The following announcements were made:

The House of Delegates meeting is to be held at 2:00 p.m., Saturday, April 12, 1975 at the Thayer Hospital, Waterville, Maine. Dinner at 1:00 p.m. will precede the business meeting.

The next meeting of the York County Medical Society will be held Wednesday, May 14, 1975 at the Webber Hospital, Biddeford, Maine with the usual format.

There were 30 physicians and 3 guests present. The meeting was then adjourned by the President.

All in all, a most enjoyable meeting was had by all.

MELVIN BACON, M.D., *Secretary*

Lincoln-Sagadahoc

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges Inn, Wiscasset, on Tuesday evening, April 15, 1975. There were twenty-nine members and guests present.

The meeting was called to order at 8:35 p.m. by the President, Dr. Ralph C. Powell. The March minutes were approved as read by the Secretary. The Secretary then read the application for active membership of Dr. Gerry S. Hayes, whose application was approved and recommended by the Board of Censors; the membership voted to accept the application.

Dr. Powell announced that Medical Care Development, Inc. is desirous of having this County Medical Society appoint a committee on screening for hypertension. There were no takers.

Dr. Robert S. Galen made a plea that non-members of the A.M.A. not throw away pamphlets which extoll the benefits of membership in the American Medical Association. He described a few of these benefits, and Dr. Richard C. Leck undergirded Dr. Galen's support.

Dr. Carl R. Griffin, Jr. described broadly a new code of laws dealing with professional liability which has been instituted in the State of Indiana. Discussion followed, which terrified the members.

Dr. Leck reported on the meetings of the Executive Committee and House of Delegates of the Maine Medical Association on the 11th and 12th of April. Several members discussed the role of the Medical Association.

Dr. Robert H. Dixon introduced Dr. Geoffrey A. Stroud, who spoke on the National Health Service in Britain.

The meeting was adjourned at 10:20 p.m.

GEORGE W. BOSTWICK, M.D., *Secretary*

Penobscot

The monthly meeting of the Penobscot County Medical Society was held on April 15, 1975 at Sing's Restaurant in Bangor, Maine.

The minutes of the March 1975 meeting were read and approved.

The meeting was opened by the President, Dr. David M. Sensenig. Dr. Sensenig introduced the guests for the evening who included Drs. Maynard Beech and Dewey Richards.

Communications received by the Society included a letter from Sen-Cit requesting the approval and endorsement of the County Medical Society for the purpose of "Health Screening 1975." Dr. John S. Houlihan made a motion, and it was seconded and passed, to postpone any endorsement of this issue until further information can be obtained from the Eastern Task Force on Aging, the parent organization of Sen-Cit.

It was noted that a questionnaire is being sent to all primary care providers by the Northeast Health Planning Council in an attempt to ascertain what is available in the area of primary care and how it presently is delivered. Dr. Thomas L. Watt, a "B" agency member, spoke to the question and encouraged completion of this questionnaire.

Under old business, the Blue Shield 80 Percent UCR Contract was again discussed. This discussion was at the direction of the membership as voted at the February 1975 meeting of this Society. Discussion then followed. All members who spoke to the question were opposed to the 80 Percent Contract, and more particularly, on the basis upon which it is founded and the possible indications and ramifications which it includes. Dr. Dexter J. Clough, 2nd made a motion, and it was seconded and passed, that we approve the 80 Percent UCR Contract only if the service benefit portion is deleted from that particular contract. Dr. Richard A. Gaillard made a motion, and it was seconded and defeated, the Blue Shield be asked to reconsider the service benefit provision of all the Blue Shield contracts.

Under new business, a report of the Interim Meeting of the House of Delegates of the Maine Medical Association, held in April 1975 at Waterville, Maine was given by Dr. John A. Woodcock. He noted that one of the highlights of the meeting was the presentation by Dr. John B. Madigan, President of the Maine Medical Association, who suggested that the Maine Medical Association consider unionization. He reported that a budget deficit would exist at the end of the fiscal year and that an increase in the dues would be forthcoming. Public Law 93-641, the law which incorporates the Health Systems Agency was also discussed at that meeting. It was voted by the House of Delegates to recommend to the Governor that one agency be designated for the State of Maine.

Dr. Edward C. Porter requested information in regard to any action which the Maine Medical Association is presently taking in the area of malpractice insurance. This became particularly pertinent since the American Medical Association in a recent communication has suggested that the State Association direct their attention to this problem as a matter of priority.

As there was no further business, the meeting was adjourned.

PHILIP G. HUNTER, M.D., *Secretary*

Kennebec

A meeting of the Kennebec County Medical Association was held on April 17, 1975 at the Augusta Civic Center. Dinner was

served to 42 members and guests, and following dinner, the meeting was called to order at 8:04 p.m. by Dr. James C. Hayes, Vice President, in the absence of Dr. Hiebel.

The minutes of the March meeting were read and accepted as read.

Old Business: The Council, having approved the application of Dr. Walter Schuyler for membership, the Association voted to accept him in fellowship.

Correspondence and Announcements: A letter from the Woman's Auxiliary requesting funds for their scholarship program was read. This matter will be referred to the Council. A letter received by Dr. Teodoro Dela Cruz from Mr. Hogerty, the Insurance Commissioner was read.

New Business: A letter from Dr. Robert W. Wilson of Jefferson requesting affiliate membership was read and the Association voted to accept his application for affiliate membership.

Dr. Hayes then introduced the speaker of the evening, Dr. Daniel Hanley, Executive Director of the Maine Medical Association, who spoke informally to the members of the Association on two subjects; the current malpractice insurance crisis and the role of organized medicine vis-a-vis the legislative process. The presentation by Dr. Hanley was most informative, and the members of the Association joined in the discussion with vigor. It is apparent that members of the medical profession must begin to work together more effectively than they have in the past in view of the many economic changes that are occurring and pressures that will be brought to bear on the health care field in the next few years.

Meeting was adjourned at 9:30 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

Somerset

A meeting of the Somerset County Medical Society was held at the Candlelight Restaurant on April 22, 1975.

Minutes of the previous meeting were read and approved.

The President, Dr. Robert W. Kaschub chaired the meeting. He read and commented on a letter he had received from the Kennebec Planning Council pertaining to prenatal care. Pertinent to the letter was the question as to whether the County Medical Profession could supply the services for patients in the area. There was considerable discussion in this regard. Discussed on this issue was patient flow from the area and the fact that patients were walking into the hospital to be delivered, never

having had any adequate medical prenatal care. Several motions were entertained.

The first motion by Dr. John P. Dow was to tell the Kennebec Planning Council to mind their business. The Society expressed the feeling that they were not interested in any further government interference in planning. The motion failed to be seconded. Following further discussion, a motion was made by Dr. Carlton E. Swett that the Kennebec Planning Council be informed by the Somerset County Medical Society that we know this problem exists, that we know the needs and we will take care of the medical problem in this regard and we do not feel that we want any more government money applied in this direction. It was seconded by Dr. Vincente L. Sy and carried.

Dr. Harland G. Turner, the delegate at the April session of the House of Delegates meeting which was held in Waterville, reported that a number of issues were discussed; pertinent issues, Medical School in Maine, Ophthalmological Drugs and the way that the State was to be divided under the Federal Law recently passed in February. There was considerable discussion regarding Federal Legislation. It was suggested that the Executive Secretary be approached in regard to having pages inserted in the Maine Medical Journal to cover pertinent legislation, either national or State level, and these pages be inserted immediately prior to publication of the magazine so that the information would be current. It was suggested that a colored page such as yellow be used to delineate this section. It was also suggested that a form be made available in this section, brief, so that the doctors may immediately relay their feelings to the Executive Secretary in regards to this pertinent legislation. It was felt that as a result of this, there would be much closer contact with the Executive Secretary in the future when quick decisions might be necessary. The Executive Secretary of the Maine Medical Association would have a more forceful working relationship with the members.

Following this portion of the meeting, members and their wives had dinner. Mr. Richard Sterns, Local Attorney, was a speaker. He discussed malpractice in the State of Maine beginning back in the 1840's. He discussed this in a most detailed manner, stating the directives that were typical in a particular era. He compared the malpractices in the past with what we were experiencing in the present day and might anticipate in the near future. This was a lengthy meeting which began at 5:30 p.m. and ended at about 11:00 p.m.

JOHN H. STEEVES, M.D., *Secretary*

PRESIDENT'S ADDRESS — Continued from Page 212

Stressing such standards in our daily lives, it follows, we must always cooperate with one another in determining and delivering the best procedures for diagnosis and treatment because, as I have said, no man can have total knowledge of all problems. Each suffering human is a very individual problem because psychomatic aspects present in all illness must alter disease patterns from patient to patient.

Ever mindful of these many philosophical truths and ever seeking to improve our knowledge and capacities for providing health care, the denouement can be nothing else but the elevation of the status of the medical profession once again to its respected pedestal.

In this day and age, such attempts at revitaliza-

tion must include concerted political efforts with a united front to propose and implement our own programs of social and medical betterment which are not geared primarily to cost controls but rather to maintaining the health of the country with the very best techniques of diagnosis and therapy.

I am sure that tremendous respect and admiration for physicians still lie dormant in the attitudes of the average American and can be brought to the surface by rededication of our profession to its ideals. Therefore, in these troubled times let us take courage, redefine and unite our efforts, and surely in the end our goals of maintaining and improving the best health care system in the world will be achieved.

Houlton, Maine 04730



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Physician Assistant in Primary Care

A. DEWEY RICHARDS, M.D.

There has been considerable discussion concerning Physician's Assistants, their value to a primary-care Physician, their effectiveness and usefulness. There has also been some apprehension on the parts of many physicians concerned with quality of care. Some Physicians have even expressed fear that we are producing "half-trained doctors" who are likely to "strike off on their own." Some Physicians feel that these men and women will not be satisfied as assistants and will attempt to assume the role of primary Physician themselves. There are also questions as to how they should be paid and how much they should be paid. These and many other questions and problems have been studied extensively by those training Physician's Assistants. The purpose of this paper is to address some of these questions and attempt to put the assistant to the primary Physician in focus.

For the purpose of this discussion, Physician's Assistants shall mean the graduate of an approved program for training assistants to the primary-care physician. This should exclude the "girl Friday," the office nurse, the medical secretary, and the medical assistants who have traditionally given the Physician a great deal of support in his practice. Although there have been reports of these people dispensing medicines and even "covering the practice while the doctor is out of town," these uses are rare. The nurse practitioner, insofar as she assists the Physician, following protocols and performing carefully delineated procedures spelled out in advance, will be considered as a Physician's Assistant. The nurse practitioner who is "practicing nursing," making "nursing diagnoses and instituting nursing treatment and care" without a Physician immediately available and knowing that he is assum-

ing responsibility for every patient seen, will not be discussed here.

Who are these Physician's Assistants about whom we are talking? They are intelligent young men and women who have completed one of several training programs designed specifically to equip them to assist a Physician. Some of these programs have as a prerequisite several years of prior medical knowledge and experience including nursing, military corpsmen duty, civilian hospital training in such areas as surgical technician, emergency ward technician, x-ray or laboratory technician and other paramedical training making them conversant and knowledgeable about many medical problems. These people, then, undergo at least one year of training, primarily in physical diagnosis with a considerable amount of additional training in recognizing common diseases and following logic pathways which direct them to appropriate treatment of the problem or referral to a Physician.

Other students with no prior medical knowledge undergo a minimal of two-years training in programs such as the one at Duke University. These courses frequently include more basic sciences and general background. It is interesting that on the National P.A. examination, there is little difference in the scores of the Physician's Assistant regardless of which pathway they took. Almost all these training programs are associated with medical schools or major teaching hospitals. The quality of the program and supervision of the Physician's Assistants in their training phase is different in each of the programs but the results are comparable.

We then have younger men and women who have received specific and careful training in many of the areas of medical care. They are usually very competent in physical diagnosis. They have a good understanding of most of the common illnesses and the

Reprint request to: A. Dewey Richards, M.D., 489 State St., Bangor, Maine 04401.

usual treatments for these. They have all had training in following directions, many with a good deal of training in the use of algorithms or logic pathways which let them arrive at a conclusion, either to institute predetermined treatment if all of the criteria are met, or to refer the patient to a Physician if there is anything unusual or not determined in the particular case. Their training universally assumes the relatively immediate availability of a Physician for consultation either by telephone, radio, or in person. Their privileges to see patients in almost every state is dependent upon a license to practice medicine held by their employer and immediate supervisor.

With the above restrictions, what is the function of these health professionals? Primarily they perform some of the multiple repetitive procedures which a Physician finds necessary in his practice. They are frequently as competent as their supervising Physician in removing casts and reapplying casts. Many have special training and capabilities in suturing minor lacerations, removing small skin lesions, and assisting in larger surgical procedures. Almost all of them have training in the usual office laboratory procedures in addition to taking electrocardiograms, performing pulmonary function testing, audiometry, tonometry, and multiple other measurements. Many have had experience in taking x-rays. All have a capability of performing complete physical examinations and obtaining meaningful complete or directed histories.

As typical of the use of Physician's Assistants in a family practice, I would like to describe the way in which the two Medexes who participate in patient care in the Bridgton Family Medical Center under the supervision of the family Physicians in that Group. In the Office they do preliminary screening on most of the acutely ill patients with simple problems such as otitis media, pharyngitis, minor trauma, upper respiratory infections and similar acute minor illnesses. Their workup is complete for these problems. In our Office, the patient is always seen by a Physician briefly, partly for purposes of precepting the work of the Physicians Assistant but more important to keep abreast of the patients and their problems. It is at this time that occasional additional problems of a psychosocial nature are also brought out.

In the Office, almost all x-rays, electrocardiograms, and pulmonary function tests are done by the Medexes. Much of the suturing and most of the cast removal and application is done by the Medexes. Physical examinations, especially those on well persons such as insurance physicals, executive physicals, camp physicals, and well-child physicals are ideally suited to the talents and capabilities of a Physician's Assistant. The list of abnormalities noted can easily be checked by a Physician with appropriate further studies or treatment ordered. In

our practice, every hospitalized patient also has a comprehensive history and physical done by a Physician's Assistant. This is dictated in detail and satisfied all the requirements for recording a detailed history and physical. All of the abnormalities and all of the findings pertinent to the patient's admission are also gone over by the admitting Physician. The complete problem list is then entered on the chart with a great deal of assurance that the dual workup is certainly far above average in thoroughness and reliability.

A Physician's Assistant can be of great value in treating patients with stable chronic illness. Patients with such problems as hypertension, obesity, diabetes, arteriosclerotic heart disease, peripheral vascular insufficiency, and multiple other problems which need to be evaluated on a regular basis can be dealt with very well by a Physician's Assistant. Originally, the Physician can program the needed care. The limits and expectations can be spelled out in advance. Deviations from these can be determined and brought to the Physician's attention for alteration of therapy or further study.

Following these patients in the Office is relatively simple for the Physician but following such patients at home or in nursing homes requires a great deal of travel time. It is in these locations that the Physician's Assistant can function to the greatest advantage. It is no longer time-consuming and wasteful for a Physician to schedule house calls on his chronically ill patients. The Medexes see these patients on a regular scheduled basis as often as their illness dictates. The changes in status can be dealt with by the Physician as the Physician's Assistant calls from each patient's home to inform the Physician of the patient's condition and findings and ask for any change in medication or treatment.

The patients in nursing homes and boarding homes, in addition to those patients in their own homes, or the homes of their family, appreciate very much the immediate availability of medical care on request in addition to the availability of regularly-scheduled visits. The Physician's Assistants also are well qualified and very useful in dealing with patients convalescing from an illness which has required hospitalization. Patients with myocardial infarctions discharged from the Hospital should certainly be seen at home within a couple of days from their discharge. Many other patients will require home visits before they are well enough to come to the Office. In the past, many of these needs were simply ignored because of the pressure of time and practice. With Physician's Assistants available, much improved medical care can be delivered on a routine basis.

In our practice, we use the Medexes very little in obstetrics and gynecology. Pelvics are done by the Physician only. The necessity of a repeat should the

Medex find abnormalities, in addition to other considerations, has led us to exclude this from the Medexes at this time. We also found that routine obstetrical checks can be done as rapidly by the Physician without the Physician's Assistant. Although our Medexes do have some experience in counseling in obesity and diabetes, most counseling is done by other paraprofessionals in our Office or by Physicians.

Patient acceptance of Physician's Assistants has been almost uniformly excellent. They appreciate the additional care which they receive. The availability of services has increased. The patient no longer fears bothering the Physician with minor problems. They enjoy the immediate availability of house calls and emergency services. The team approach to medical care of which our Medexes are a part, offers many advantages to most of the patients and they readily recognize and appreciate this.

Our Medexes have extensive experience in acute trauma. They are equipped with an emergency kit including intravenous fluids and most of the common emergency drugs. They can respond to calls as the paramedics in "Emergency" with radio contact with the Office and Hospital. Usually on such a call, a Physician would accompany them, but they do a very creditable job in emergency care with radio or telephone instructions from a Physician.

Physician's Assistants such as the Medex and other similarly-trained and utilized paraprofessionals can be a significant factor in improving patient care. Almost universally, the Physicians who have utilized these paraprofessionals have felt that the quality of care increased. The quantity of care given each patient also increases. With time, a Physician's usefulness can be extended in a community with some increase in quantity of patients treated and a definite increase in quality of care rendered.

Studies of patient acceptance of the Physician Assistant have been done. The studies done in my practice show that which is obvious to those who work with Physician's Assistants, that almost all patients appreciate the increased services and thoroughness with which their problems are dealt. Although we have been carefully tuned to any possible complaints by our patients, almost all the feedback has been positive.

Physician's Assistants satisfaction with their roles has also been studied. The careful selection of the candidates for Physician's Assistants in the Dartmouth Medex New England program has resulted in all of their graduates with whom I have come in contact being extremely well satisfied with their position and station in life. They enjoy the patient care and the appreciation expressed by the patients to them. They get many of the emotional benefits of a primary-care Physician with very little

of the responsibility. They are generally well paid, at about the level of a supervisor of nurses. It is my feeling that a rare individual will have the necessary resources, energy, and desire to return to college, go to Medical School, and become a Physician. This should happen with about the same frequency that it occurs in nursing and other similar professions.

The problem of adequate supervision is important both to the Physician's Assistant and their preceptors. A Physician's Assistant who is properly trained and reasonably knowledgeable, would not put himself in a position where he does not have the immediate supervision of a Physician. In most states, a Physician's Assistant can not function legally without a responsible Physician. The Physician assuming responsibility, knowing he would be liable for any malpractice by the Physician's Assistant, must insist that the Physician Assistant perform within the carefully prescribed limitations. Any Physician's Assistant who is practicing without adequate supervision is practicing medicine without a license for which there are strict laws and penalties in every state. Those of us who are most familiar with the usefulness of these persons would also be the most critical of anyone practicing independently and thereby endangering livelihoods of all those similarly trained.

In all those practices with which I am aware, several things occur which were not predictable. Initially, with the increased service to the same number of patients for the same amount of money, the net profit falls precipitously upon arrival of the Physician's Assistant. The increased patient load which results after a few months, eliminates the loss of income, and most Physicians who have had an assistant more than two years find their income as high as it was prior to having a Physician's Assistant. A second observation which also was not predicted is the increased load upon the Physician who has an assistant. Rather than giving more spare time and making it easier for him to leave his practice for postgraduate study and recreation, he finds himself working at a more cerebral level when he is working with increased responsibility for an ever-increasing number of patients. These negative aspects are compensated for by the improved patient care which results and the increased availability of services to the patients who are served by the practice. With only one exception, the Physicians who have added a Physician Assistant to their practice have felt the quality of patient care increased immediately. This, plus the stimulation of having a questioning paraprofessional to teach, compensates for some of the immediate losses in income and increased responsibility.

In summary, the Physician's Assistant is a very useful adjunct to the health-care team. In a practice

Continued on Page 239

Management of Thyrotoxicosis

IVOR M. D. JACKSON, M.D.

Thyrotoxicosis is a syndrome resulting from excess circulating thyroid hormone. The syndrome is most commonly associated with Graves' disease, a disorder of unknown etiology characterized by some combination of diffuse goiter, eye changes, and dermatopathy. Neonatal Graves' disease describes a thyrotoxic state, usually self-limited, occurring in infants born to mothers with Graves' disease. This rare condition is thought to result from transplacental passage of Long Acting Thyroid Stimulator (LATS), or a similar immunoglobulin, which stimulates thyroid hyperfunction in the fetus.¹

The three major therapeutic approaches to Graves' disease are: antithyroid drugs, radioactive iodine (¹³¹I), and thyroidectomy. The choice of therapy depends upon the patient's individual needs and the physician's experience and training. Frequently more than one approach could be considered therapeutically sound. This review deals primarily with the drug management of Graves' disease, but alternative modes of therapy and other causes of thyrotoxicosis will be mentioned as well.

DRUG TREATMENT OF THYROTOXICOSIS*

Antithyroid Agents: Thionamides

The two most important antithyroid drugs, propylthiouracil (PTU) and methimazole (Tapazole®), are in the class of thionamide compounds. These agents prevent thyroid hormone synthesis by inhibition of the coupling of the iodotyrosines; they probably also inhibit the oxidation and organic binding of thyroid iodide.² They do not prevent uptake of iodide by the thyroid gland. Peak plasma concentrations of methimazole are reached within one hour of an oral dose. The apparent disappearance half-time is approximately 6 hours.³ The half-time of PTU is even shorter. Since these drugs are eliminated from the body fairly rapidly, frequent dosage

is recommended to produce adequate therapeutic effects. The usual initial dose of PTU is 100 to 150 mg every 8 hours, or 10 to 15 mg of methimazole every 8 hours, although in occasional patients once-daily dosage is adequate.⁴ A normal metabolic state is usually reached within 6 to 8 weeks. Rarely, doses as high as 1200 mg per day are needed by patients with large goiters and severe toxicity. When large daily doses are administered, it may be beneficial to reduce the dosage interval to 4 hours, since drug metabolism may be accelerated due to the thyrotoxicosis. Shorter dosage intervals and lower unit doses may also be preferable in less toxic individuals. A thyrotoxic patient taking 100 mg of PTU twice a day, for example, may occasionally be rendered euthyroid by changing the dosage regimen to 50 mg every 6 hours.

Although higher doses will produce a euthyroid state more rapidly, the risk of drug toxicity is increased. True resistance to the thionamides probably does not occur, and therapeutic failures are usually attributable to patients taking their medication irregularly. However, patients whose thyroid glands are rich in iodine (from prior ingestion, or administration during diagnostic radiological procedures) may respond to treatment relatively slowly, since thionamide drugs inhibit the synthesis, but not the release, of thyroid hormone.

PTU, but not methimazole, also has an extra-thyroidal action of blocking the peripheral conversion of thyroxine (T₄) to triiodothyronine (T₃). This may be of importance in the overall antithyroid effect of this agent,⁵ particularly in thyrotoxic crisis.

Effect of Treatment. The thyroid gland will decrease in size and vascularity in about 50% of patients receiving antithyroid medication. In some, however, the morphology of the gland will be unchanged, and in a few the thyroid increases in size. Enlargement of the gland usually indicates over-treatment and is corrected by a reduction in dosage. It may also signal exacerbation of the underlying disease which necessitates an increase in dose. Clinical findings and measurement of circulating thyroid hormone levels usually resolve these possibilities.

Thyrotoxic patients being treated with anti-

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*See Table 1

TABLE 1
DRUGS USED TO TREAT THYROTOXICOSIS^a

<i>Drug Category</i>	<i>Mode of Action</i>	<i>Initial Dosage</i>	<i>Specific Indications</i>	<i>Major Hazards</i>
<i>Corticosteroids^b</i> Prednisone	? suppression of immunoglobulin stimulation of the thyroid	10 to 120 mg orally every 6 hours	Ophthalmopathy; Thyrotoxic crisis	Complications of steroid therapy
Hydrocortisone		400 mg per day IV by infusion or in divided doses		
<i>Monovalent Anions</i> Potassium perchlorate	Blocks thyroid trapping of iodide	200 mg every 6 hours	No longer used in clinical medicine	Aplastic anemia
<i>Thionamides^c</i> Propylthiouracil (PTU)	Blocks (1) organification of iodide and (2) coupling reaction	100 to 150 mg orally every 8 hours	Maintenance therapy in thyrotoxicosis. Useful for thyrotoxic crisis in higher doses	See Table 2
Methimazole		15 mg orally every 8 hours		
<i>Iodine</i> Potassium iodide (SSKI)	Blocks release of thyroid hormone from the thyroid (in some glands — see text — also inhibits organification)	50 to 100 mg (1 to 2 drops) orally every 8 hours	Adjunctive to thionamides prior to thyroidectomy; thyrotoxic crisis (higher doses often used)	Skin reactions; interference with ¹³¹ I studies; "Jod-Basedow effect"
Sodium iodide		1 to 2 gm per day by IV infusion		
<i>Lithium</i> Lithium carbonate	Blocks release of thyroid hormone (cf. iodine)	600 to 1200 mg per day orally in divided doses	Possible alternative to thionamides in patients who are allergic	Numerous hazards associated with serum concentrations above 1.5 mEq/liter
<i>Adrenergic Antagonists</i> Propranolol	Blocks peripheral effects of thyroid hormone without altering thyroid function test	20 to 80 mg orally every 4 to 8 hours; 1 to 5 mg IV every 4 hours	Symptomatic therapy of thyrotoxicosis and thyrotoxic crisis	Cardiac failure; bronchospasm
Reserpine		0.25 mg orally every 8 hours; 2.5 to 5 mg IM every 8 hours		
Guanethidine		10 to 50 mg orally every 8 hours		
<i>Sedative-Hypnotics</i> Phenobarbital	Increases elimination of thyroid hormone through enhanced biliary excretion	30 to 60 mg orally 3 times a day	When sedation is needed	Excess central nervous system depression

^a The drugs are categorized in relation to their site of action and not in order of therapeutic importance (see text).

^b Corticosteroids also lower T₃ levels by an unknown peripheral action.

^c PTU also inhibits the peripheral conversion of T₄ to T₃.

thyroid drugs should be monitored routinely for blood concentrations of both T_4 and T_3 . T_4 concentrations may fall into the normal range relatively quickly, while T_3 concentrations remain elevated and thyrotoxic symptoms persist. Normalization of both T_4 and T_3 levels is required. This phenomenon is distinct from the syndrome of " T_3 thyrotoxicosis"⁶ in which the untreated gland appears to produce normal amounts of T_4 but excess quantities of T_3 .

Once a euthyroid state has been achieved, the antithyroid medication can be reduced initially by about one third. Then every three to four weeks the medication can be reduced gradually to maintenance dosage (100 to 150 mg/day of PTU or 10 to 15 mg/day of methimazole). In some clinics sodium levothyroxine (Synthroid, [®] Letter [®]) in doses of 0.2 mg/day is routinely combined with antithyroid drugs. The antithyroid medication can then be given with less careful monitoring and in larger doses with less hazards of hypothyroidism.⁷ This combination therapy does not alter the progress of the eye changes of Graves' disease, except inasmuch as it prevents hypothyroidism which may severely exacerbate the ophthalmopathy (see below).

Length of Treatment. A typical course of antithyroid therapy lasts one to two years. Antithyroid treatment per se probably does not alter the underlying disease, but rather controls the disease until spontaneous remission takes place. Remission is more likely if pituitary-thyroid feedback inhibition returns to normal, and if the gland is small and diminishes in size during antithyroid medication. The thyroid suppression test may allow prediction of remission or relapse following cessation of drug treatment.⁸

The one-hour oral ^{131}I uptake, which is not influenced by coadministration of thionamide drugs,⁹ is a potentially useful modification of the thyroid suppression test. The test is done with the patient pretreated for 7 to 10 days with thyroxine, 0.2 mg/day. If the one-hour uptake exceeds 10%, the chance of relapse on stopping the antithyroid drugs is greater than 95%. An uptake between 4 and 10% has a 73% of remission, and an uptake of less than 4% has an 87% chance of remission.

Antithyroid medication should be gradually withdrawn, since this allows relapse to be detected before the antithyroid effect is completely lost.¹⁰ If relapse occurs after drug withdrawal, then alternate forms of therapy should be considered (see below), but control of the thyrotoxicosis should initially be achieved by reintroduction of the thionamide. In one series, 54% of 176 patients with thyrotoxicosis had a remission lasting 6 to 20 years following a course of treatment.¹¹

Adverse Reactions. Skin rashes occur in approximately 5% of patients and may be macular, papular

or urticarial. They are usually pruritic and often develop about two weeks after therapy is started. Sometimes these dermatologic reactions are self-limited and disappear despite continuation of the drug.

The most serious adverse effect is agranulocytosis; it is occasionally associated with a polyarteritis or lupus-like syndrome.¹² Premonitory symptoms of agranulocytosis include fever and sore throat. Should such an illness develop, patients should report it to their physician and be advised to stop the drug immediately. Regular white blood counts are rarely helpful in anticipating this condition. If agranulocytosis occurs, the drugs should be immediately discontinued and steroid therapy initiated. Recovery almost invariably occurs, but the same drug should not be given again. Although it has been suggested that an alternative drug may then be given a cautious trial,¹⁰ the likelihood of the same event occurring with a different thionamide is about 50%. It is probably more reasonable to initiate other antithyroid measures.

The polyarteritis-like syndrome of arthralgias, skin rashes and fever usually responds satisfactorily to discontinuation of the offending drug and to administration of steroids. The incidence of this syndrome can be very high when large doses of thionamides are given.^{12,13}

Other adverse reactions include fever, arthralgia, myalgia, neuritis, thrombocytopenia, cholestatic hepatitis, enlargement of lymph nodes and salivary glands, and toxic psychoses. These reactions may reflect an occult autoimmune syndrome and suggest that therapy should be changed.¹⁰ Other symptoms such as hair loss and altered taste sensation occur, but it is not established whether these are due to the drug or to the underlying disease. Propylthiouracil, but not methimazole, is rarely associated with prothrombin deficiency.

I recommend that if a minor side effect occurs, an alternative thionamide drug should be given, with consideration of other forms of treatment such as radioiodine (^{131}I) or thyroidectomy. The adverse effects of PTU and methimazole are summarized in Table 2.

Other Antithyroid Drugs With Actions Similar to the Thionamides

These drugs include the aminoheterocyclic group and the substituted phenols. Para-aminosalicylic acid (PAS, an antituberculous agent), and the sulfonyleureas (oral hypoglycemic agents) are aminoheterocyclic drugs. Resorcinol, a cutaneous antiseptic, and salicylamide, an analgesic drug, are substituted phenols.

Although these agents are not potent antithyroid agents by themselves, they may potentiate the effects of PTU or methimazole. They are *not* used

TABLE 2

ADVERSE EFFECTS OF THIONAMIDE DRUGS

<i>Adverse Effect</i>	<i>Comment</i>
Skin rashes	Macular, papular or urticarial, pruritic; 5% incidence but rises with larger doses
Agranulocytosis	Serious side effect; usually preceded by fever and sore throat; dose-dependent; incidence less than 0.5%
Polyarteritis or lupus-like syndrome	Generalized vasculitis with arthralgia, neuritis, lymphadenopathy. May be associated with skin rashes and granulocytopenia; probably dose-dependent
Myalgia, arthralgia, hepatitis, thrombocytopenia	May be part of a generalized vasculitis
Hypoprothrombinemia	Effect of propylthiouracil; caution if anticoagulant also being given
Dysgeusia; alopecia	May be due to the drug or the underlying disease

specifically as antithyroid drugs in thyrotoxicosis.

Antithyroid Drugs That Inhibit Iodide Transport

These agents are monovalent anions which inhibit the trapping of iodide by the thyroid gland. Drugs in this group (e.g., potassium perchlorate) are no longer used in the treatment of thyrotoxicosis because of their severe toxicity, such as irreversible aplastic anemia¹¹ and the nephrotic syndrome. Unlike the thionamides, their antithyroid effect can be overcome by iodine administration.

Iodine

Prior to the introduction of thiouracil,² iodine was the major antithyroid agent available. Its principal therapeutic effect is to reduce the release of thyroid hormone from the thyroid gland. In untreated hyperthyroid patients given 150 mg (3 drops) of a saturated solution of potassium iodide (SSKI) per day, there is incomplete and unsustained clinical improvement.¹⁵ However, if given to thyrotoxic patients previously treated with ¹³¹I, potassium iodide (KI) is effective in controlling thyrotoxicosis. This is probably attributable to inhibition of organic iodine formation.¹⁶

The antithyroid effect of iodine occurs more rapidly than that of the thionamides. Thus iodine is valuable in the treatment of thyrotoxic crisis (see below), and in situations in which an intravenous antithyroid agent is needed since no parenteral preparation of the thionamides exists.

Following the achievement of a euthyroid state with PTU (or methimazole), KI (150 to 300 mg/day) is usually given along with the thionamide for 7 to 10 days prior to thyroidectomy. This decreases the vascularity of the thyroid gland. It has been suggested that stopping the thionamide prior to surgery and giving iodine alone may occasionally precipitate thyrotoxicosis ("Jod-Basedow effect"). This prob-

ably occurs only when thionamide therapy has been inadequate.

Iodine therapy has disadvantages. Since it competitively inhibits thyroid uptake of ¹³¹I, it prevents use of radioiodine therapy for some weeks. Furthermore, if iodine is given alone, stores of thyroid hormone will build up and delay the antithyroid effects of subsequently administered thionamide. Iodine may precipitate thyrotoxicosis ("Jod-Basedow effect") if given to a euthyroid patient with a goiter¹⁷ or to a patient previously treated with a thionamide for thyrotoxicosis.¹⁸

The dose of iodine as iodide needed for control of thyrotoxicosis is approximately 6 mg/day.¹⁰ Thus, doses of KI in the range of 3 to 6 drops (150 to 300 mg) daily are quite high and should not normally be exceeded except in thyrotoxic crisis (see below). Toxic reactions to iodine occur, especially with large doses. They include skin rashes, drug fever, sialadenitis, conjunctivitis, rhinitis, conditions resembling polyarteritis such as thrombotic thrombocytopenic purpura, and a leukemoid eosinophilia.¹⁰ If these reactions occur, the iodine should be stopped.

Lithium

Lithium and iodine are the only agents in clinical use that influence hormonal iodine release from the thyroid gland. Interest in lithium as an antithyroid agent was aroused following reports that this drug occasionally caused goiter with hypothyroidism in psychiatric patients being treated for manic-depressive psychosis.¹⁹

In one study lithium carbonate in doses of 800 to 1200 mg/day was found effective in controlling thyrotoxicosis in patients refractory to other therapy.²⁰ In other studies, however, thyroid "escape" was frequent and concurrent administration of a thionamide was required for lithium to be effective.²¹ Serum lithium levels must be closely monitored and kept between 0.5 and 1 meq/liter. Higher levels may cause serious side effects; these include tremor, ataxia, dizziness, confusion, coma, anorexia, nausea, vomiting, diarrhea, cardiac arrhythmias, and circulatory collapse.

Lithium carbonate is not a drug of first choice, but may represent an alternative agent for the treatment of thyrotoxicosis if allergy to the thionamide drugs exists. Further studies of its effectiveness are required.

Adrenergic Antagonists

Many of the symptoms and signs of thyrotoxicosis are at least partly secondary to apparent sympathetic overactivity. This can be antagonized by agents that deplete the tissues of catecholamines (reserpine or guanethidine), or that block the response at receptor sites (β -adrenergic blockers,

such as propranolol). Reserpine is given orally in doses of 0.25 mg every 8 hours or intramuscularly, in severe cases, in doses as high as 2.5 to 5 mg every 4 to 8 hours. Guanethidine is given orally in doses of 50 to 150 mg/day; such doses may cause marked postural hypotension.²²

The most valuable agent appears to be propranolol. Effective doses range from 10 mg every 8 hours up to 40 to 80 mg every 6 hours. It is most effective in reducing heart rate, and occasionally in lessening tremor, anxiety, and stare. In severe cases it may be given intravenously with electrocardiographic monitoring in doses of 1 to 5 mg. The rate of intravenous administration should not exceed 1 mg/min, and not more than 5 mg should be given in a 4-hour period.

Since thyroid function tests are not altered by propranolol, it can be started as soon as the clinical diagnosis has been made. Propranolol does not interfere with the action of the antithyroid drugs; therefore, it can be given concurrently with PTU or methimazole. Propranolol has a prompt action and has been reported to be effective in rapidly reversing myopathy,²³ bulbar palsy,²⁴ and upper motor neuron signs²⁵ before any improvement in thyroid function tests has taken place.

Relative contraindications to propranolol include cardiac failure and bronchial asthma, and the most important adverse effects are precipitation of these conditions. Other adverse reactions include gastrointestinal disturbances, peripheral vascular insufficiency, allergic reactions, and a variety of central nervous system symptoms including confusional states.

Steroids

In theory immunosuppression is a rational approach to Graves' disease since thyrotoxicosis appears to result from thyroid stimulation by LATS, an immunoglobulin.¹ In one study large doses of prednisone alone produced remission of hyperthyroidism in a group of patients with Graves' disease.²⁶ This provides a basis for the adjunctive use of steroids in thyrotoxic crisis. Steroids in high doses are also effective in severe ophthalmopathy. Other immunosuppressive agents such as azathioprine have been relatively ineffective in Graves' disease.

Because of serious adverse effects, steroids should *not* be used as first-line therapy. Pharmacologic doses of steroids lower circulating T₃ levels by an unknown mechanism.²⁷ This peripheral action could partly explain the antithyroid effect of steroids, especially in thyrotoxic crisis.

Phenobarbital

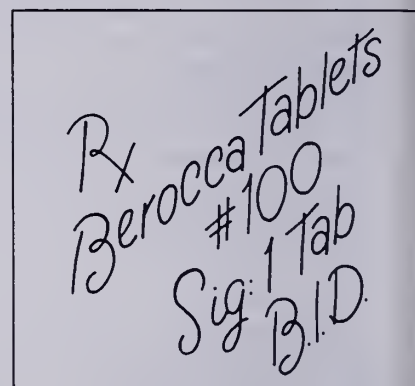
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Continued on Page 230

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of thyroid hormones by inducing enzymes in the smooth endoplasmic reticulum. It may also increase the rate of peripheral turnover of thyroid hormones and lower serum levels.²⁸ The usual dose is 30 to 60 mg every 8 hours. It is only supplementary to other antithyroid agents.

THYROTOXIC CRISIS

Thyrotoxic crisis ("thyroid storm") is decompensated thyrotoxicosis. It is an unusual but extremely serious complication of partially treated or untreated hyperthyroidism.^{28,29} It most commonly occurs following thyroidectomy in a patient whose thyrotoxicosis was inadequately controlled prior to surgery, or in a patient with severe thyrotoxicosis complicated by an intercurrent disease or infection. In view of the high mortality associated with thyrotoxic crisis, doses of antithyroid agents are much higher than those normally prescribed in the outpatient management of thyrotoxicosis.

Therapeutic efforts are directed towards inhibition of thyroid hormone release and synthesis, and antagonism of sympathetic overactivity. Supportive measures include treatment of hyperpyrexia and cardiac failure. Propylthiouracil is given by mouth or by nasogastric tube in doses of 200 mg every 4 hours during the first 24 hours. One hour following the initial dose of PTU, iodine, the most important therapeutic agent at this time, is administered. PTU is given *first* to prevent repletion of the thyroid hormone stores in the gland by the subsequent iodine. Iodine is given as SSKI, 10 drops (500 mg) every 4 hours, or as 1 to 2 gm of sodium iodide every 24 hours by continuous intravenous infusion. The antisympathetic agent propranolol is given by oral or parenteral routes in the doses described. Reserpine is usually beneficial only when given parenterally. Although these agents have the potential to precipitate cardiac failure in patients whose cardiac compensation depends upon sympathetic stimulation, some reports have suggested that both reserpine³⁰ and propranolol³¹ may actually improve the cardiac efficiency of patients with thyrotoxic heart disease. Because reserpine has sedative effects, it is particularly useful in agitated patients, but undesirable for lethargic or depressed individuals. Propranolol is hazardous in patients with asthma, diabetes mellitus, or underlying cardiac disease, particularly if cardiac failure exists.²⁸ Digitalis therapy and diuretics are indicated for cardiac disease with pulmonary edema. Steroids in high doses, i.e., 100 mg of hydrocortisone intravenously every 6 hours, are helpful in a general sense, as well as for reasons mentioned earlier. A further indication for steroid administration is possibly associated adrenocortical insufficiency.³² Fever is treated with wet packs, fans and tepid sponging. Salicylates should probably be avoided. Like thyroid hormone,

salicylates act as uncouplers of oxidative phosphorylation and may conceivably exacerbate the underlying problem. Furthermore, aspirin increases free T₃ levels in the serum by displacement of T₃ from thyroxine binding globulin (TBG).³³

Once the condition is under control, the doses of antithyroid agents should gradually be reduced to the usual maintenance levels in preparation for more definitive therapy.

TREATMENT OF OPHTHALMOPATHY

Proptosis and infiltrative ophthalmopathy occur in thyrotoxicosis due to Graves' disease, but not in toxic nodular goiter (Plummer's disease). Treatment of thyrotoxicosis is often associated with lessening of the proptosis, but occasionally the proptosis increases markedly. For the common symptoms of mild irritation in the eyes, hydroxyethyl cellulose artificial tears (Adorbotear[®]) — (0.44% in polyvinyl pyrrolidone 1.67%) should be applied as eye drops 3 to 4 times per day. Other measures such as raising the head of the bed at night, eye patches if diplopia or impaired lid closure are present, and diuretics are also used. For advancing proptosis with impairment of visual acuity, high doses of steroids (prednisone up to 120 mg/day) may dramatically arrest the process.³⁴ Retro-orbital injection of steroids are also helpful. If steroids fail, orbital decompression may be required.³⁵ It is critically important that patients treated for thyrotoxicosis, especially those with some degree of exophthalmos, do not become hypothyroid, since this may lead to malignant exophthalmos. Treatment of thyrotoxicosis concurrently with thyroid replacement, as described earlier, may prevent such an occurrence.³⁶ The medical management of the ophthalmopathy of Graves' disease was recently reviewed by Ivy.³⁷

TREATMENT OF DERMOPATHY

Pretibial myxedema occurs in association with finger clubbing and exophthalmos. The skin lesions can be treated with local steroid therapy such as 0.1% betamethasone (Valisone[®]) ointment under occlusive dressings, or with flurandrenolide dressing on plastic tape (4 ug per sq cm) (Cordran[®] tape).

CHOICE OF THERAPY IN GRAVES' DISEASE

Most patients with thyroid overactivity (especially if surgery is contemplated) should first be rendered euthyroid with PTU or methimazole. This prevents complications such as exacerbation of thyrotoxicosis from ¹³¹I-induced radiation thyroiditis, and reduces the possibility of thyrotoxic crisis after thyroidectomy. Mild cases of thyrotoxicosis can be treated initially with radioiodine alone, but in more severe cases an interim antithyroid drug may be needed, since radioiodine takes 2 to 6

months to work. In patients who have completed childbearing and have no more than a moderate sized goiter, radioiodine is the definitive treatment of choice. With large goiters, surgery must be considered. With younger adults a full course of 12 to 24 months of therapy with a thionamide is indicated since a prolonged remission may be obtained. The thyroid suppression test gives some indication of the probability of remission.⁸ If a patient relapses, control should again be achieved with a thionamide, and surgery or radioiodine then given. The choice often depends as much upon the competence of thyroid surgeons in a particular medical center as upon one's attitude toward radiation exposure during childbearing years.^{10,38}

The choice of therapy for children is controversial; antithyroid drugs, thyroidectomy, and radioiodine have been advocated. The successful treatment of thyrotoxicosis with ¹³¹I in 87 children and adolescents followed for 5 to 24 years has been reported.³⁹ No cases of cancer, leukemia, or altered reproductive capacity were noted. However, I recommend treating such patients with courses of antithyroid drugs, including sympathetic antagonists, and to delay more definitive therapy beyond the age of 20. Such management may be altered by individual situations such as drug allergy, failure to take tablets regularly, etc.

HYPERTHYROIDISM AND PREGNANCY

This problem is also controversial. Radioiodine therapy is contraindicated because ¹³¹I crosses the placenta. I recommend managing patients with small doses of antithyroid drugs; this approach appears to be relatively free of complications. However, antithyroid drugs cross the placenta readily and can cause goitrous hypothyroidism in the fetus. Concomitant thyroid medication for the mother should probably be avoided, since thyroid hormone crosses the placenta poorly and will necessitate increased antithyroid medication for the mother. Surgery has its advocates, but it is associated with an increased incidence of abortion. Iodine therapy given prior to thyroidectomy crosses the placenta and may cause a goiter in the fetus. There have been recommendations for treatment solely with propranolol.⁴⁰ Since antithyroid drugs are secreted in the milk, patients on such therapy should not breast-feed. Thyrotoxicosis in pregnancy is reviewed elsewhere.^{41,42}

TREATMENT OF THYROTOXICOSIS IN CONDITIONS OTHER THAN GRAVES' DISEASE*

Neonatal Graves' disease usually, but not invariably, is self-limited and should be controlled with

TABLE 3
CLASSIFICATION OF THYROTOXICOSIS

Condition	Special Features
Graves' disease	Associated eye changes; dermopathy
Neonatal Graves' disease	Self-limited; usually remits in 3 to 4 months
Toxic mono- or multinodular goiter	Long standing goiter; eye signs usually absent
"Jod-Basedow" (Iodine-induced thyrotoxicosis)	Pre-existing goiter; recent administration of iodine
Subacute thyroiditis	Tender goiter; thyroid ¹³¹ I uptake low
Thyrotoxicosis factitia	Ingestion of excess thyroid hormone; thyroid ¹³¹ I uptake low
Neoplastic disease	Presence of extra-thyroidal tumor tissue; secretion of a TSH-like material, as in choriocarcinoma
Hypothalamic-pituitary disease	Possible pituitary fossa enlargement; serum TSH elevated
Metastatic toxic thyroid carcinoma	Concentration of ¹³¹ I by neoplastic tissue
Struma ovarii (teratoma)	Ectopic thyroid tissue in ovarian tumor; thyroid gland ¹³¹ I uptake low

the usual antithyroid drugs at doses adjusted for body weight. For PTU the initial dose is 4 mg/kg, and for methimazole one tenth of that. The maintenance dose is half the initial dose.

Toxic multinodular goiter is usually managed like diffuse goiter of Graves' disease, although spontaneous remission is unlikely to occur following thionamide therapy unless the condition represents Graves' disease superimposed on a long-standing multinodular goiter. The thyroid scan can sometimes be helpful in making this distinction.¹⁶ Thyrotoxicity from a single nodule can be treated satisfactorily with ¹³¹I, using doses larger than that required for Graves' disease. Surgery is preferred by some as being more reliable in effecting a cure.¹⁶

Iodine-induced thyrotoxicosis ("Jod-Basedow effect") is sometimes produced by iodine administration to euthyroid goitrous subjects, and is cured by iodine withdrawal.¹⁷ Thyrotoxicosis during subacute thyroiditis is short-lived and usually mild; sympathetic antagonists, salicylates or steroids can be given as indicated.⁴³ Treatment of thyrotoxicosis factitia depends upon establishing the diagnosis. The management of thyroid-stimulator secreting neoplasms, especially choriocarcinoma, involves management of the primary condition as well as the thyrotoxicosis.⁴⁴ Hypothalamic-pituitary disease causing thyrotoxicosis is recognized by measurement of elevated serum thyroid stimulating hormone (TSH) levels.⁴⁵ Treatment of the excess TSH excretion will cure the hyperthyroidism. Metastatic toxic thyroid carcinoma should be treated with ablative doses of radioiodine; the associated thyrotoxicosis is usually mild. Treatment of struma ovarii causing thyrotoxicosis consists of surgical removal of the ectopic tissue. Radioiodine ablation may be effective in such cases.

*See Table 3

SUMMARY

The treatment of thyrotoxicosis with thionamide drugs (propylthiouracil or methimazole) usually allows restoration of a normal metabolic state within 6 to 8 weeks. Important side effects include skin rashes, agranulocytosis, and a generalized vasculitis or lupus-like syndrome. Other antithyroid agents include lithium and iodine; the latter agent is primarily used in thyrotoxic crisis and in preoperative preparation for thyroidectomy. Sympathetic antagonists (propranolol, reserpine and guanethidine) control thyrotoxic symptoms and are valuable in crisis therapy. High doses of steroids are also useful in thyrotoxic crisis.

A course of thionamides (1 to 2 years) may produce a long remission, especially in those with a small goiter, but in patients who have completed childbearing, ^{131}I is usually given as definitive therapy. Large goiters in younger patients should probably be treated by thyroidectomy. The best management in childhood or pregnancy is not established, but thionamide therapy, at least initially, is recommended.

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Longevity of American Physicians

COR DE HART, M. D.*

The question is frequently asked, do physicians live longer than the general population?

In order to study this question, more than 37,000 death notices of physicians reported were reviewed in the *Journal of the American Medical Association* for the years 1961-1971. About 7% of the names in the death notices were female. For statistical purposes, we have excluded the female population and we have considered the population consisting of mainly white physicians because of the small non-white physician population.

Mortality statistics for white men for the year 1968, as reported by the Division of Vital Statistics of the National Center for Health Statistics, were used for general population figures. The ages at death of 879, 884 white men were compared with those of the physicians.

The populations were distributed in 5-year intervals. The percentages and cumulative percentages were calculated.

between physicians and the general white male population. The cumulative percentages are respectively 49.13 percent and 48.96 percent. But from age sixty-five on until the age of eighty, the five-year group percentages are higher for white men in the general population than for physicians.

From the age of eighty and above, comparatively more physicians die. This means that physicians in general, die later.

Of the total white male population, 21.7 percent expects to reach eighty years and over. In the physicians this is 25.2 percent, which is a very significant difference. ($p, <0.00001$)

Of the total white male population, 3.33 percent expects to reach ninety years and over, in the physicians this is 4.89 percent, which also is a very significant difference. ($p, <0.00001$)

In the five-year age groups between the ages thirty-five and sixty-four, a greater percentage of physicians die than in the general white male population.

TABLE 1

COMPARISON OF AGE OF DEATH, ALL CAUSES, FOR PHYSICIANS AND WHITE MEN IN THE GENERAL POPULATION

AGE	White Men, USA (1968)			Physicians, USA (1961-1971)		
	Number	Percent	Cumulative Percent	Number	Percent	Cumulative Percent
95 and over	5717	0.65	99.99	372	1.00	99.99
90-94	23544	2.68	99.34	1443	3.89	98.99
85-89	60000	6.82	96.66	3129	8.44	95.10
80-84	101732	11.56	89.84	4423	11.93	86.66
75-79	127865	14.53	78.28	4811	12.97	74.73
70-74	128682	14.62	63.75	4747	12.80	61.76
65-69	113148	12.86	49.13	4468	12.05	48.96
60-64	98401	11.18	36.27	4159	11.21	36.91
55-59	76768	8.72	25.09	3417	9.21	25.70
50-54	54334	6.18	16.37	2298	6.20	16.49
45-49	36266	4.12	10.19	1591	4.29	10.29
40-44	22436	2.55	6.07	1043	2.81	6.00
35-39	12987	1.48	3.52	593	1.60	3.19
30-34	8751	0.99	2.64	365	0.98	1.59
25-29	9253	1.05	1.05	226	0.61	0.61
Totals	879884	99.99		37085	99.99	

The significance of the differences between physicians and the general white male population were calculated.

RESULTS

When we analyze the data in Table 1, it appears that for the age groups up to age sixty-five, there is no difference in the cumulative percentage of deaths

between physicians and the general white male population ($0.02 > p > 0.01$). Note also that in the age group twenty-five to twenty-nine, a greater percentage of white men die than physicians. This difference appears to be significant. ($p, <0.00001$)

SUMMARY

Death notices of physicians were reviewed in the *Journal of the American Medical Association* over the years 1961-1971. The ages of death of 37,085

*Courtesy Staff, Thayer Hospital, Waterville, Maine 04901.

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Glucagon Assisted Air-Barium Contrast Colonography in a Small Hospital Setting

ROBERT L. BURDICK, M.D. and RUSSELL V. RADCLIFFE, M.D.

INTRODUCTION

Recent estimates from the American Cancer Society predict that carcinoma of the colon and rectum will be diagnosed in approximately 99,000 Americans this year, and in that same span of time roughly 48,000 Americans will die of that disease.¹ The absolute 5-year survival rate for early lesions is 71%, contrasted to 13% survival for advanced lesions.² In recent years, general surgeons have accounted for a significant improvement in the 5-year survival rate by using the "no touch technique."³ Radiologists now have an opportunity to improve early diagnosis by the technique to be described below, and thereby further improve the over-all survival rate.

The limitations of the barium enema examination are well known to every practicing radiologist. Because of overlapping loops of colon, colon spasm, poor bowel preparation, and overlapping reflux into the terminal ileum, the barium enema examination can often do little more than exclude generalized mucosal abnormalities or large neoplastic lesions. At least one researcher has reported that over 18% of carcinomas of the colon are completely missed for these reasons on the initial barium enema examination, thus contributing to delay in diagnosing colon carcinoma.⁴ In a separate review, 75% of such errors were considered to have resulted from inability of the radiologist to find the lesion because of poor bowel preparation.⁵ Presumably all of these patients had symptoms prompting the initial barium study. A false negative report in this clinical situation is worse than no study at all, because it lulls the well-intended clinician into the unjustified impression that the colon is probably normal.

RECENT DEVELOPMENTS

Several recent developments have combined to offer the radiologist an opportunity for a significant technical advance over previous barium enema examination procedures. The first of these is hypotonic colonography. Hypotonic colonography has been performed for some time with the assistance of Probanthine,[®] but Probanthine sometimes results in urinary retention in both males and females, and risks aggravation of glaucoma. Recently the radiology literature has been filled with numerous articles^{6,7,8} indicating the safety and effectiveness of glucagon for relaxing colon musculature, provided that glucagon is not given to a brittle diabetic or

patient with suspected pheochromocytoma or insulinoma. As long as no more than 2 mgs. is given intramuscularly, less than 10% of patients can be expected to have side effects, and these are usually limited to nausea. Predictable bowel relaxation will occur in most individuals within 10 to 15 minutes.

The other major technical advance is a thorough revision of the air-barium enema procedure per se, largely through the thoughtful efforts of Doctor Roscoe Miller, Professor of Radiology at the University of Indiana. Dr. Miller lists five requirements as basic to his technique, and these are:⁹

- (1) A clean colon.
- (2) Suitable barium suspension that will coat well and not bubble or precipitate.
- (3) Adequate insufflation of the bowel with air.
- (4) Drainage of excess barium from the rectum.
- (5) An adequate number of films with good radiologic technique.

THE BASIC TECHNIQUE⁹

Adequate colon preparation, perhaps the most important requirement, can be routinely accomplished using the Miller Protocol. This requires a combination of low residue diet, laxatives, and enemas. Dr. Miller recommends a specific low residue diet* beginning on the evening of the third day prior to the examination. This low residue diet is continued until examination time, and moderately strong laxatives are used on the day prior and two days prior to the examination. These are either 2 ounces of castor oil, 2.5 ounces of X-Prep liquid, or sometimes 10 ounces of Magnesium Citrate or 20 gms. of Magnesium Sulfate. A large volume of oral liquids must also be given to assist an effective purge: a full 8 ounce glass of liquid each hour for 6 to 7 hours the day preceding the examination has been found adequate.

In addition to laxatives, Dr. Miller administers a 2,000 milliliter water enema given by the Department of Radiology immediately prior to the examination. To allow for effective cleansing, at least a one-half hour wait following the cleansing enema is routine prior to beginning the barium procedure.

Two mgm. of glucagon is administered I.M. 10 minutes prior to beginning the barium examination.

The suitable barium suspension, requirement #3 above, is quite different than the mixture traditional-

*copies available (upon request) from authors.



Fig. 1A and 1B are horizontal beam, cross table right and left lateral decubitus views of the recto-sigmoid colon, demonstrating the excellence of visualization of the rectum and adjacent sigmoid colon.

ly used. Normal barium enema techniques use relatively dilute barium, in the expectation that (unless the bowel is quite large) a high kilovoltage x-ray technique will penetrate the barium column, revealing otherwise obscured neoplasms. Therefore, approximately a 1/3 weight to volume mixture (or less) is normally used. Dr. Miller has found instead that a 65% weight to volume mixture is most desirable,¹⁰ giving a thickness approximately that of sour cream. The advantage of such a thick mixture is that excellent coating will be achieved prior to air insufflation, and maintained afterwards.

Once the mixture of thick barium and air (50 to 75 squeezes of a standard sphygmomanometer bulb) have been administered with the patient primarily in a prone position (it is necessary to manipulate the patient into various oblique and lateral positions for proper coating), the barium enema bag is lowered and excess barium contained in the rectum is allowed to return to the barium bag. If this technique is properly executed, anatomic visualization of the rectum by x-ray will equal or surpass that which can be seen by sigmoidoscopy (Fig. 1). The examination is performed with the patient mostly in the prone position so that barium reflux into the terminal ileum will not occur. In most individuals, the ileo-cecal valve is directed posteriorly and medially from the cecum, and with the patient in a prone

position barium is less likely to fill the terminal ileum.

An enema tip especially designed to facilitate rectal drainage¹¹ is used, although it is possible to perform the entire examination with only a straight tip with a "Y" connector.

Once proper coating has been accomplished, 14 x 17 inch films are taken. These include a prone sigmoid view, PA film, prone 20 degree RAO and LOA, and a right lateral view including the rectum. Then the supine, 20 degree LPO and 20 degree RPO are taken, all three to include both colonic flexures. Next both lateral decubitus films are taken. Following this, upright spot films are taken of each flexure, transverse colon, and cecum, as needed. Fluoroscopic films are then taken of any area which appears deserving of further study.

DISCUSSION

The entire scope of this technique, with its promise of earlier detection of limited stages of colon carcinoma by avoidance of errors was presented at the Radiology Society of North America Annual Convention in Chicago in December 1974. Because of the potential impact of this technique, we have attempted to employ this air contrast colon examination as a primary examination under the following circumstances, as recommended by Dr. Miller:⁹

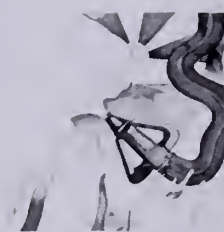


Fig. 2. Routine sigmoid view showing excellent visualization.

- (1) Any patient with rectal bleeding for any reason or a verified history of bleeding.
- (2) Polyps on protoscopic examination.
- (3) A previous history of polyps or carcinoma.
- (4) A strong family history of polyps or carcinoma.
- (5) A high index of suspicion on the part of the clinician or radiologist based on a change in bowel habits, weight loss, unexplained anemia, or other reason.

Presumably because this is a new technique and because of the obvious extra effort required in bowel preparation, acceptance by the referring medical community has been cautious, but interested. Since mid-January 1975, we have accomplished 30 of these examinations at the St. Joseph Hospital, and have in at least one case demonstrated early ulcerative colitis that was not apparent on the initial, standard barium examination. The technique does not appear to be appropriate for patients who could not withstand the bowel preparation, such as those suspected of being obstructed, perforated, or having toxic megacolon. On the other hand, patients who are unexpectedly found to be obstructed or severely spastic in the course of a

Continued on Page 237



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Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

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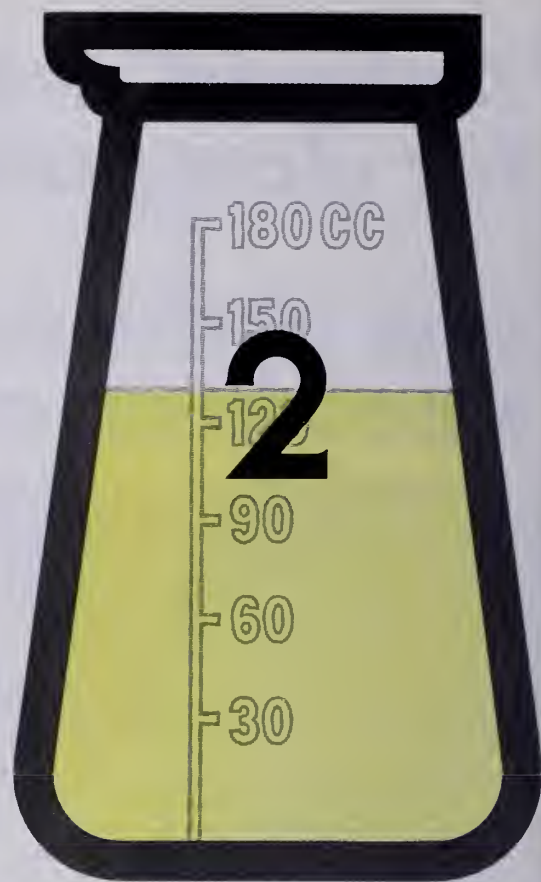
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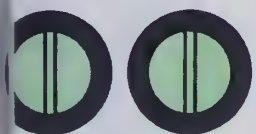


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Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprolthrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

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* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium fre-

quently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy

patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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conventional barium enema examination will often prove to be anatomically normal except for minimal spasm following administration of 2 mgs. of glucagon intramuscularly. Since some colon spasm is encountered normally in the course of a barium enema examination, glucagon pre-medication permits a more comfortable, thorough examination. Moreover, we have never encountered loss of barium on the examination table in a patient who has been pre-medicated with glucagon, and we have never had to inflate a Bardex (retainer balloon) in any of these patients. Consequently, we often use glucagon as a supplement to a conventional barium enema to facilitate a more comfortable, thorough exam. The effect on the post evacuation film has been negligible.

We have modified the thick barium preparation as described above so that we use a 100% weight to volume mixture. This ensures that when the colon is distended with air there will still be adequate coating. We have found that approximately 40 to 50 squeezes of a standard sphygmomanometer bulb produces adequate colon distention. The number of radiographs advocated by Dr. Miller certainly results in a thorough examination. We have often found it unnecessary to do additional fluoroscopy following the standard radiographs, described above.

The patients in general have no difficulty following the low residue diet, although we have made it a policy to ask the patient to come to the X-ray Department for a thorough discussion of the procedure in general before beginning the preparation, and at this time we have emphasized the importance of strict adherence to the diet.

The over-all result in bowel preparation with the above diet, fluid ingestion, and laxative use has frequently been so effective that it has not been necessary to give the final cleansing enema immediately prior to the examination. In fact, we find that when it is necessary to use this final enema, a small amount of residual water is invariably present and this dilutes the concentration of barium, somewhat deteriorating the quality of the examination. In some selected instances, we have been able to perform the glucagon assisted examination one day following a conventional barium enema examination, if the colon was well prepared for the initial examination. This is usually accomplished with one dose of additional laxative and a cleansing enema.

In general we have found that the entire examination occupies one fluoroscopy room for almost one full hour, approximately double the time required for a conventional examination.

CONCLUSIONS

(1) Visualization of every aspect of the colon is achieved which cannot be matched by conventional barium enema examinations (Fig. 2). With the technique of rectal drainage and cross table lateral radiography, even the rectum is well studied down to the rectal verge.

(2) Patient acceptance of the bowel preparation procedure has been generally favorable.

(3) Patients who have had a previous conventional enema find that the addition of glucagon to the regimen results in a much more comfortable procedure.

(4) Although we have not in fact identified otherwise undiagnosed polyps or other growths, the improved visualization assures that we are definitely not overlooking any such abnormalities. Other centers using this technique have improved their detection rate for early lesions: Dr. Miller has shown one case of a polyp arising on the superior surface of one of the valves of Houston, not seen on sigmoidoscopy.

(5) Most referring clinicians are agreeable to transferring the responsibility for thorough bowel preparation (in an individual, selected patient) to the radiologist, and this has not been a source of contention with referring clinicians.

(6) The entire examination is easily managed in a small community hospital, and should therefore, be easily practiced in every hospital.

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- Miller, R. E.: The Barium Enema as a Cancer Detection Procedure: Its Use and Abuse, Syllabus — Categorical Course on Radiology of Gastrointestinal Tract Disease, R.S. N.A., December 1974.
- Miller, R. E.: Barium Sulfate Suspensions. *Radiology* 84: 241, 1965.
- Miller, R. E.: A New Enema Tip. *Radiology* 92: 1492, 1969.

Dr. Burdick, 171 Washington St., Brewer, Maine 04412
Dr. Radcliffe, 297 Center St., Bangor, Maine 04401

Special Article

COMMUNICATIONS

State of Maine
EXECUTIVE DEPARTMENT
Augusta, Maine
04330

June 16, 1975

To the Honorable Members of the House of Representatives and the Senate of the 107th Maine Legislature

A great American, whom I admire, kept a saying on his desk: "The buck stops here." Since this Legislature, after back-and-forth debate, has seen fit to place the key decision regarding the future of a medical school for Maine in my hands, I accept the consequences of an extremely difficult choice. I am vetoing L. D. 773, AN ACT to Authorize the University of Maine to Proceed With the Development of a School of Medicine as Part of the Teaching Program of the University System.

I therefore request in the interests of fiscal responsibility and to avoid a recurrence of an L. D. 1994 type situation, as well as to help restore our favorable bond rating, that you sustain this veto.

While I had previously indicated my opposition to a medical school, my respect of the Legislature and my desire to be fair to proponents and the University caused me to step back and spend countless hours of my own time plus that of my staff and volunteer citizens in reevaluating the total situation. As a result of this time and research, I am electing to veto this bill because of the following specific reasons:

(1) The Legislature has passed and sent to the Governor a bill which calls for a substantial present and future commitment of the State's resources to the establishment of a medical school, while failing to appropriate the funds necessary to accomplish this purpose. In other words, the Legislature has not appropriated any money in the current services budget to pay for the school. Approval of this bill could mean a further erosion of already tight operating funds or a future tax increase. Furthermore, this Governor can ill afford the luxury of approving bills which have been submitted to him without an allocation of cost or appropriation by the Legislature. Furthermore as a result of my experience as Governor, I do not want to be unfair to future Governors or Legislatures and approve bills without appropriate costs or price tags. This Legislature and this Governor have paid the price of that approach.

(2) The cost estimates presented by proponents of the school are not realistic, and fail to project

costs to the State of Maine for adequate faculty, future building and/or capital equipment needs, as well as costs to the State in the event that federal funds are eliminated or cut back. I have a strong feeling that Maine cannot afford in the future another cost estimate mistake such as occurred with L. D. 1994. This also could happen here.

(3) There was no conclusive evidence presented which shows that a medical school will solve Maine's doctor shortage in rural areas. It is my understanding that many of the more expert in the medical and health care fields believe that the solution to the doctor shortage in Maine lies in the development of residency programs, and not a medical school. Further, we should in this regard improve our efforts to aid new doctors in overcoming the many difficulties associated with the establishment of practices in rural areas.

(4) As Governor, I want to help the University. However, to add an additional burden involving program and finances could severely hinder the University at this time. There is some evidence already that time and dollars spent promoting and lobbying for a medical school have hurt the present University program and budget.

In addition, I have strong reservations about the form of this legislation in that the medical school would come under the jurisdiction of the present Board of Trustees of the University of Maine, which I feel has its hands full getting its own financial house in order.

(5) I am also advised that additional spaces are available for our medical students at out-of-state institutions and much lower costs would be possible utilizing these programs. Statistics also show that 54.2% of Maine residents who graduated from the University of Vermont School of Medicine under the Regional Medical Student Program administered by the New England Board of Higher Education, returned to Maine to practice medicine during the years from 1958 to 1973. Our research also indicates that proponents either did not understand, or failed to recognize and report this fact, plus evidence that the University of Vermont and other medical schools will now be able to accept more Maine students. Ironically, and unfortunately, Maine's gain in this regard is Massachusetts' loss as these additional openings reportedly are primarily attributable to that state's financial problems which were caused in part when costs associated with the University of Massachusetts Medical School mushroomed beyond the cost projections promulgated by those who promoted the School.

This is because Massachusetts has indicated that due to their financial crisis and cost over-runs on their medical school, they are going to have to use funds to support their medical school as contrasted with supporting students in other medical schools.

Even though I am vetoing this measure, I pledge:

(A) To conduct an intensive campaign to attract and retain doctors in Maine.

(B) To attempt to locate resources to subsidize doctors and other health care professionals in our rural areas.

(C) To proceed immediately with New Hampshire and Vermont to explore the possibility of developing a regional medical school facility and program.

(D) To continue efforts already started to get doctors to move to Maine's rural areas from other states. I have already made initial contact with medical schools and the Maine Medical Association in

this regard.

(E) We should also explore the possibility of asking one of our fine private institutions to develop a medical education program. This would protect the University from further erosion of its undergraduate efforts and also give the taxpayers the advantage of the greater budgetary scrutiny which occurs in the private college sector which contrasts with the tendency of a state university to go to the taxpayers whenever they make a mistake or need more money.

While realizing that many members supported the medical school legislation in good faith, for the above reasons I again respectfully ask that my veto be sustained.

Very truly yours,
JAMES B. LONGLEY
Governor

JBL:bh

PHYSICIAN ASSISTANT IN PRIMARY CARE — *Continued from Page 223*

where authority can be delegated, these people improve the quality of care immediately. With understanding of their role by themselves and the super-

vising Physicians, there is little likelihood that any abuses will occur.

Bridgton Family Medical Center, Bridgton, Maine 04009

The Doctor's Agency

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NOYES & CHAPMAN

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EDWARD D. NOYES III

From the Secretary's Notebook

Summary of 1975 Annual Meeting of the M.M.A. House of Delegates June 14, 15 and 16, 1975 at Rockport, Maine

The 122nd annual session of the M.M.A. House of Delegates was held at the Treadway-Samoset Resort in Rockport, Maine, with a registered attendance of seventy-six delegates and alternates, and thirty-nine guests. The first session was held on Saturday at 2:00 P.M., the second session on Sunday at 2:00 P.M., and the third on Monday at 4:45 P.M. John B. Madigan, M.D., President of the M.M.A., called to order the meetings of the House, which were presided over by George W. Bostwick, M.D., Speaker of the House.

Election of Speaker and Vice Speaker of the House of Delegates for 1975-76 — George W. Bostwick, M.D., was re-elected Speaker of the House, and Richard M. Swengel, M.D., Vice Speaker of the House.

Budget for 1976 — The reference committee recommended that the Budget, as presented be approved, with the added recommendation that the Executive Committee go over it, line by line, giving an especially hard look at *The Journal*, and this was *voted*. The Executive Committee will report back to the House of Delegates, hopefully in December.

Supplemental Budget — The reference committee recommended that **dues** be set at \$200 per member (in order to hire additional personnel), and that the Executive Committee be empowered to levy \$100 per member for the acquisition of new office space and equipment for the M.M.A. There was considerable discussion on the assessment. A vote was taken on raising the dues to \$200, beginning on January 1, 1976. A majority were in favor, with only 2 dissenting votes, and the motion *carried*. A motion was made to authorize the Executive Committee to issue an assessment, **up to \$100 per member**, for the purposes of capital improvement if there is a need for it, and the motion was *approved*, with 8 dissenting votes.

Committee on Nominations — A slate was presented in April at the Interim Meeting of the House of Delegates and at this meeting for vote, and the following officers elected:

President-Elect

Richard C. Leck, M.D.

Executive Committee

2nd District — Douglas R. Hill, M.D.

4th District — Richard T. Chamberlin, M.D.

9th District — Benoit Ouellette, M.D.

Dr. John W. Wickenden of Rockland was elected to complete Dr. Leck's term on the Executive Committee for the 3rd District.

AMA Delegate

Robert E. McAfee, M.D.

AMA Alternate Delegate

Brinton T. Darlington, M.D.

The Standing Committees, as recommended by the Committee on Nominations, were *approved*, with the exception of the Ethics and Discipline Committee (final decision on the makeup of this committee to be made by the Executive Committee). Dr. Warren Baldwin of Portland was suggested for the Peer Review Committee.

Reports (not included in the House of Delegates' folder) —

Executive Director — In executive session, Dr. Hanley spoke to the delegates on the subjects of Utilization of medical and hospital services, problems of ethics and discipline, fees and medical malpractice insurance in Maine.

Diabetes — Dr. Melvin Bacon, Chairman, read a lengthy report. The House *voted* acceptance of this report and copies are available from Dr. Bacon or the M.M.A. office.

Printed reports not requiring action (resolutions from committees appear elsewhere in this summary), and *accepted* for information were as follows: Committees — Allied Health Professions, Amy W. Pinkham Fund, Conservation of Vision, AMA-ERF, Maternal & Child Welfare, Medicine & Religion, School Health, Emergency Medical

Service and Computer Utilization in Medical Practice; Reports of Secretary-Treasurer, President of the Woman's Auxiliary, Executive Committee members, Delegates to Out-of-State Medical Society meetings.

RESOLUTIONS

Malpractice — Submitted by Penobscot County, a substitute resolution was presented by the Reference Committee and *approved* as follows:

WHEREAS, there has been a significant rise in the premium rates for medical malpractice insurance and a recent crisis of availability in Maine, and

WHEREAS, these costs add significantly to the increased cost of patient care, and

WHEREAS, the medical malpractice crisis threatens to impair the physician-patient relationship,

BE IT RESOLVED that the Maine Medical Association:

1. Endorses the establishment of a Medical Malpractice Commission for Maine. The Association stands prepared to cooperate in the Commission's effort to examine the medical malpractice liability problem and to assist in the development of remedial legislation effecting appropriate changes in Maine law. This legislation should assure the equitable compromise of all conflicting interests and guarantee the availability of malpractice insurance at reasonable rate.
2. Establish a Patient Injury Prevention Committee to collect the necessary data, identify the causes of all patient injuries and to recommend programs and methods to reduce them to a minimum.

Automated Financial Services — The original resolution was submitted by the Committee on Computer Utilization in Medical Practice and the following substitute resolution presented by the Reference Committee, was *approved*:

WHEREAS the administrative demands of medical practice are an increasing burden to Maine Physicians,

THEREFORE BE IT RESOLVED that the MMA support the Committee on Computer Applications in evaluating and encouraging automated financial services.

Fluoridation — Presented by the Reference Committee, at the request of the Committee on Maternal & Child Welfare, the following resolution was *approved*:

WHEREAS studies have shown that fluorida-

tion of water reduces the incidence of teeth decay and has the support of the American Medical Association and American Dental Association,

THEREFORE BE IT RESOLVED that the M.M.A. reaffirms its support and encourages action on Fluoridation of all public water supplies in the State, and

THEREFORE BE IT FURTHER RESOLVED that a copy of this resolution be sent to the president of the M.D.A., Commissioner, Dept. of Health, Education and Welfare, and County Medical Societies.

Neonatal Intensive Care Center — This resolution from the Committee on Maternal and Child Welfare, resolving that the M.M.A. "compliments the Maine Medical Center on the development and continued improvement of the neonatal intensive care center at the Maine Medical Center," was *rejected*. This was the reference committee's recommendation because they felt it was unnecessary to spend time on such a resolution.

Nutritionist for the Dept. of Health and Welfare — This resolution was also presented by the Committee on Maternal and Child Welfare. It asked that the M.M.A. recommend "that the Department of Health and Welfare employ a nutritionist to fill the vacancy on its staff." The Reference Committee felt they did not have enough information to go on and recommended that this be referred back to the Committee for further study and recommendations and this was *so voted*.

School Health — This resolution was prepared by the Reference Committee, as suggested by the School Health Committee in its report, and *approved* as follows:

WHEREAS Health Education is vital to any school's education curriculum,

BE IT RESOLVED that the M.M.A. continues its support of the School Health Committee in its effort of promoting health education through its cooperation with State and local committees, and

BE IT FURTHER RESOLVED that a copy of this resolution be sent to the Commissioner, Department of Education and Culture Services, and to the Division of Public Health Nursing.

Report of Reference Committees — Recommendations (not listed elsewhere in this summary), as *approved* by the House of Delegates, are as follows:

Burn Committee — The report was *approved*, with an added expression of support of the House of Delegates in the Committee continuing its present efforts.

Mental Health Committee (revised report) —

The recommendations that paragraphs 1, 2, 3 & 5 of the report be filed for reference was *approved*. It was suggested and *approved* that paragraph 4, and paragraph 6 (sections a, b & c) be *referred* back to the Committee for specific recommendations to be made to the M.M.A. Executive Committee. Paragraph 6 (section d) was *approved*.

Committee on Care of the Disadvantaged — A request from the Chairman of this Committee that the name be changed to the Committee on Rural Medicine was presented by the Reference Committee and *defeated*. A further motion that the Executive Committee be instructed to see that bylaw amendments are presented next year to change the name of this committee to the Committee on Urban and Rural Health was also *defeated*.

Continuing Education Committee — A recommendation that the written report, and the supplemental oral report be accepted, with approbation for the work done by the Committee, was *approved*.

Peer Review Committee — The written report, and supplemental oral report, as recommended by the reference committee, was *approved* with commendation.

Bylaws Committee — This lengthy report, which was initially presented to the House of Delegates at its April meeting, was *approved* as presented, with considerable discussion on the part dealing with the Committee on Nominations. Revised bylaws for the M.M.A. will be printed, and a copy sent to each member of the Association.

Report of Executive Committee Chairman — The written report was *accepted*. Dr. Leck added that the resolution presented to the House of Delegates in April by the York County Medical Society, asking that the M.M.A. publish a **legislative newsletter**, was discussed at length by the Executive Committee. No funding mechanism accompanied the resolution, as is now required, and the Executive Committee felt the newsletter would be too costly to be done now. Androscoggin County has what it feels is an effective mechanism for disseminating legislative information to their members that is sent out from the M.M.A. The Executive Committee's recommendation was that other counties also be responsible for disseminating legislative material to their members, and this was *approved* by the House of Delegates.

Maine Blue Cross and Blue Shield Award of Appreciation — The award this year went to Dr. John F. Gibbons of Portland.

A. H. Robins Community Service Award — The

Community Service Award for 1975 was presented to Dr. Robert F. MacBride of Lubec.

Out-of-State Delegates — The following delegates spoke briefly of the major problems in their respective states and extended greetings: Dr. Bernard O. Nemoitin, Connecticut; Dr. Frank Kennedy, II, New Hampshire; Dr. Russell Hager, Rhode Island; Dr. John P. Byrne, Massachusetts; and Dr. Harry M. Rowe of Vermont.

Award by Continuing Education Committee — Dr. Richard T. Chamberlin, Chairman, reported that an Accreditation Program for CME has been developed by this Committee and it has been accepted by the AMA so that all accrediting work done within the State carries full weight of Category I for four years. Dr. Donald Marshall accepted the CME Award in behalf of the Maine Medical Center — the first institution to be surveyed by the M.M.A. Committee.

Reporting of Infectious Diseases — Dr. Peter Leadley, Director of the State Bureau of Health, showed some slides that represented planning being done for the reporting of infectious diseases, and asked the delegates to take this information back to their county societies. He outlined the current reporting mechanism being proposed, the reporting forms to be used, etc. Further information will be sent in the mail to all the county societies from Dr. Leadley's office.

Special Memberships — The recommendations for special memberships were *approved*.

Medical School for Maine — Following recess of the Saturday meeting of the House of Delegates, Governor James B. Longley met with the delegates to discuss the Medical School for Maine bill which is waiting on his desk for his signature or his veto. The Governor's initial comments were that he was not going to leave a deficit for his children and nothing is free. What is the **real** cost of a medical school for Maine, where is the money going to come from, and is it the best way to spend our money in rural health? The Governor believes we can solve the problems of rural health, but he's not sure the medical school is the only way. The discussion with Governor Longley lasted about an hour, with physicians giving their personal thoughts on why the bill should or should not be given approval.

At Sunday's meeting of the House of Delegates, Dr. Donald Robertson of Milbridge reported that a committee was formed this a.m., consisting of Drs. John Woodcock, George Bostwick, Linus Stitham, John Madigan, Robert MacBride, Charles Hannigan, Louis Bove and himself — because they felt the

physicians should be willing to raise \$100,000 minimum to advance the idea of a medical school. In 2 hours the committee received pledges of \$18,000 and the committee will be soliciting more pledges from the members — which they hope will give them some leverage to approach the legislators with a request that a veto of the medical school be overridden, if the Governor decides to veto the bill. If no medical school develops, the pledges will not be called, Dr. Robertson added. Another meeting of the House of Delegates was suggested for Monday to discuss the Medical School for Maine — regardless of whether the Governor decides to sign the bill or veto it — and a motion was made to this effect and *approved*.

At the time of Monday's session of the House, it still was not known what the Governor's decision was in regard to the Medical School bill. Dr. Leck chaired this meeting and asked for a discussion on what action the Association should take to group present programs of medical education — particularly if the medical school bill is vetoed. Discussions were held earlier today with those physicians involved with the Family Practice residency programs in Maine, and it was the general feeling that 13 FP residency graduates a year are needed to keep close to the attrition rate in Maine. It is strongly felt by those involved with the residency programs that medical school affiliation is needed 1) to get accreditation of these programs and 2) to get funds for these programs. Some feeling was expressed that support of FP residency programs couldn't be given in place of a medical school, and it was also suggested that rather than accept an alternative to a medical school now, that efforts for the school could

be made another year in the legislature. After considerable discussion, a motion was made to refer this subject to the Executive Committee for study and to make recommendations, with the impetus that we are to push forward for a medical school. This was *approved*.

P.L. 93-641 — National Health Planning and Resources Development Act of 1974: Dr. Robert Andrews asked for a discussion of this Act, and asked that the possibility be considered of the M.M.A. applying for designation as the Health Systems Agency in the State. Dr. Hanley stated that at the April meeting of the House, we were instructed to assist with the development of a HSA, and two meetings have been held of the various health groups in the State. It was discovered that there is a concerted effort on behalf of certain groups for creating another H.S. Agency in the State. We are now trying to get the two groups together as one, for the development of one Health Systems Agency for the State.

Stenographic Record — A summary of the proceedings of the House of Delegates is being sent to the county presidents, and to the members of the House of Delegates. (The complete report is on file in the Association's office in Brunswick, where it is available to any member of the Association.)

The meeting was recessed at 4:00 P.M. on Saturday, June 14; at 6:00 P.M. on Sunday, June 15, and adjourned at 5:45 P.M. on Monday, June 16.

PATRICIA A. BERGERON
Secretary-Treasurer, M.M.A.

DRUG THERAPY REVIEWS — *Continued from Page 232*

43. Papapetrou, P. D., Jackson, I. M. D.: Thyrotoxicosis due to 'silent' thyroiditis. *Lancet* 1: 361-363, 1975.
44. Karp, P. J., Hershman, J. H., Richmond, S., Goldstein, D. P., Selenkow, H. A.: Thyrotoxicosis from molar thyrotro-

- pin. *Arch Intern Med* 132: 432-436, 1973.
45. Emerson, C. H., Utiger, R. D.: Hyperthyroidism and excessive thyrotropin secretion. *N Engl J Med* 287: 328-333, 1972.

LONGEVITY OF AMERICAN PHYSICIANS — *Continued from Page 233*

physicians were compared with those of 879,884 white men in the general population.

Up until the age of 65, there were no significant differences for age of death between the two groups.

For physicians who reached the age of 65, there is an increased life expectancy.

3327 Rockfield Dr., S., Wilmington, Delaware 19810

President
Maine Medical Association
1975-1976



EUCLID M. HANBURY, JR., M.D.

Euclid M. Hanbury, Jr., M.D. of Belfast, Maine became the 126th President of the Maine Medical Association at the 122nd annual session banquet on June 16, 1975. He has represented his District on the Executive Committee of the Maine Medical Association since 1971. He has, additionally, served on the M.M.A. Peer Review Committee since its formation in 1971, and on the Health Finance Committee for two years, 1973-1975, serving as chairman the last year.

Dr. Hanbury was born in Portsmouth, Virginia on February 14, 1927, son of Euclid M. and Blanche C. Hanbury. He attended Virginia Military Institute in 1943-44, Hampden-Sydney College in 1947, Duke University in 1948 and received his medical degree from the University of Virginia Medical School in 1952. He interned in medicine and surgery at the Royal Victoria Hospital in Montreal from 1952 to 1953, was a Special Fellow in Medicine and Resident Fellow in Thyroid Physiology at the Sloan-Kettering Institute in New York from 1953 to 1954, was Assistant Resident and Research Fellow in Surgery at the University of Virginia Hospital from 1954 to 1957, was a Fellow in Surgery at the Lahey Clinic in Boston from 1957 to 1958, and was a Senior Assistant Resident (1958-59) and Resident Surgeon at the University of Virginia Hospital (1959-1960). He was also an Instructor in Surgery at the University of Virginia from 1960 to 1963, Director of Medical Education at the Portsmouth General Hospital in Virginia from 1963 to 1968, Director of Isotope Laboratory at the Portsmouth General Hospital in Virginia from 1964 to 1968, and Co-director of the Renal Dialysis Unit at Portsmouth General Hospital in Virginia from 1966 to 1968. In 1968, Dr. Hanbury relocated in Belfast.

He is certified by the American Board of Surgery and is a member (and former Secretary-Treasurer) of the Waldo County Medical Society, the Maine Medical Association, the American Medical Association, the American Thyroid Association, the American Association for the advancement of Science and the New York Academy of Science.

He and his wife, Kathleen, and three-year-old son, Luke, reside in Bayside, Maine. His extra medical interests include choral music, sailing and flying.

Executive Committee Members Elected at the 122nd Annual Session of the Maine Medical Association

Rockport, Maine

June 14-17, 1975

President

EUCLID M. HANBURY, JR., M.D.
Belfast

President-elect

RICHARD C. LECK, M.D.
Bath

Ninth District

BENOIT OUELLETTE, M.D.
Fort Kent

Second District

DOUGLAS R. HILL, M.D.
South Portland

Delegate to AMA

(Jan. 1, 1976 to Jan. 1, 1978)
ROBERT E. MCAFEE, M.D.
Portland

Third District

JOHN W. WICKENDEN, M.D.
Rockland

Alternate Delegate to AMA

(Jan. 1, 1976 to Jan. 1, 1978)
BRINTON T. DARLINGTON, M.D.
Augusta

Fourth District

RICHARD T. CHAMBERLIN, M.D.
Executive Committee Chairman
Waterville

Speaker of the House

GEORGE W. BOSTWICK, M.D.
Newcastle

Dr. Richard C. Leck was elected President-elect, Dr. Douglas R. Hill was re-elected to the Executive Committee (Second District) for a three-year term, Dr. John W. Wickenden of the Third District was elected to complete Dr. Richard C. Leck's unexpired term (1974-1977), Dr. Richard T. Chamberlin was re-elected to the Executive Committee (Fourth District) for a three-year term and elected to serve as Chairman for 1975-1976, and Dr. Benoit Ouellette was re-elected to the Executive Committee (Ninth District) for a three-year term. Dr. Robert E. McAfee was elected Delegate to the AMA and Dr. Brinton T. Darlington, Alternate Delegate to the AMA. Dr. George W. Bostwick was re-elected Speaker of the House of Delegates.

DR. LECK of Bath was born in Newark, New Jersey on February 12, 1931, son of Walter C. and Katharine T. C. Leck. He was graduated from the University of Chicago in 1955 and received his medical degree from the University of Chicago School of Medicine in 1959. Dr. Leck interned at the University of Chicago Clinics from 1959 to 1960 and served a residency in Pediatrics for two years. From 1962 to 1964, he served in the U.S. Air Force as Captain and then served a residency in Pathology at the University of Colorado Medical Center from 1964 to 1968. Dr. Leck practiced at the St. Anthony's Hospital in Rock Island, Illinois and the Moline Public Hospital in Moline, Illinois from 1968 to 1970 when he located in Bath. He practices Pathology in the Bath-Brunswick area.

He is a member of the Lincoln-Sagadahoc County Medical Society, the Maine Medical Association and the American Medical Association, and is certified by the American Board of Pathology. Dr. Leck has served on the M.M.A. Executive Committee since June 1972, and chairman for 1974-75. He has also served on the Budget Committee.

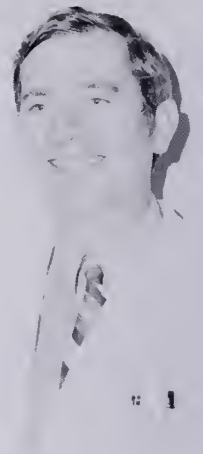
DR. HILL of South Portland was born in Portland on April 22, 1927, son of Carlos L. and Vivian L. Hill. He was graduated from South Portland High School in 1945, Bowdoin College in 1950, and received his medical degree from the University of Rochester School of Medicine in 1954. Following an internship and



DR. HILL



DR. WICKENDEN



DR. CHAMBERLIN

residency at the Rhode Island Hospital in Providence, Dr. Hill began practice in South Portland. He is certified by the American Board of Family Practice. Dr. Hill has served on the Executive Committee since 1974.

He is a member of the Cumberland County Medical Society (and former President), the Maine Medical Association, the American Medical Association, and the American Academy of Family Physicians.

Dr. Hill, his wife and children reside in Cape Elizabeth.

DR. WICKENDEN of Rockport was born in New Haven, Connecticut on August 16, 1940, son of Grover B. and Olwen W. Wickenden. He was graduated from Yale University in 1962 and received his medical degree from Yale University School of Medicine in 1966. Dr. Wickenden interned at the San Francisco General Hospital from 1966 to 1967, and served a residency in Orthopedic Surgery at the Long Beach Veteran's Hospital from 1967 to 1968. He served two years as a Major in the U.S. Army Medical Corps at Fort Hood Army Hospital in Texas. Following a two-year residency in Orthopedic Surgery at Yale University, he located in Rockland.

He is a member of the Knox County Medical Society, the Maine Medical Association, the American Medical Association, and is an associate member of the Maine Academy of Orthopedic Surgeons and a candidate for membership as a Fellow of the American Academy of Orthopaedic Surgeons.

Dr. Wickenden is affiliated with the Knox County General Hospital (Penobscot Bay Medical Center after September 1975), where he is on the Professional Activities Committee. He is on the consulting staff (Orthopedic Surgery) at the Waldo County General and Miles Memorial Hospitals.

His major interests outside of Orthopedic Surgery are political: medical and the Republican party. He is Director of the Camden Y.M.C.A., on the Development Committee of the Penobscot Bay Medical Center, and President of the Penobscot Bay Physicians' Building, Inc., a group of physicians who have developed a professional building adjacent to the Penobscot Bay Medical Center.

DR. CHAMBERLIN, who resides in Clinton has served on the M.M.A. Executive Committee since 1971.

Dr. Chamberlin was born in Randolph, Vermont on October 5, 1930, son of Paul P. and Pauline L. Chamberlin. He was graduated from Colby College with a B.A. degree in 1952 and received his medical degree from Tufts University School of Medicine in 1956. Following an internship at the Indiana University Hospitals from 1956 to 1957, he served two years in the U.S. Navy Medical Corps as a Lieutenant. He served a residency at the Boston City Hospital (Tufts) from 1959 to 1961 and the Boston V.A. Hospital, Jamaica Plains from 1961 to 1962.

He was a Teaching Fellow in Medicine at Tufts from 1960 to 1962; on the Active Staff, Internal Medicine, at the Thayer Hospital and Seton Hospital, and the Consultative Staff at the Central Maine Sanatorium from 1962 to 1970; Director of Extended Care and Social Medicine at the Thayer Hospital from 1967 to 1969; Director of Continuing Medical Education, Upper Kennebec Valley from 1969 to 1971; Director of Continuing Care and Director of CME at the Thayer Hospital from April 1971 to the present. Dr. Chamberlin has been involved in Peer Review and PSRO in Maine from its start and is currently President of the Pine Tree



DR. OUELLETTE



DR. MCAFEE



DR. BOSTWICK

Organization for Professional Standard Review, Inc. He also is chairman of the M.M.A. Committee on Continuing Education and the Peer Review Committee.

He is a member of the Kennebec County Medical Association, the Maine Medical Association and the American Medical Association. Dr. Chamberlin is also a member of the Maine Society of Internal Medicine, the Maine Thoracic Society, the American Geriatrics Society, the American Congress of Rehabilitation Medicine, the American Thoracic Society and the American Society of Internal Medicine. He is on the Board of Directors of the Maine Lung Association, the Kennebec Valley Mental Health Center, and the PTOPSR.

DR. OUELLETTE of Fort Kent was born in Baker Lake, New Brunswick, Canada on June 8, 1925. He was graduated from St. Joseph University in Moncton, New Brunswick and received his medical degree in 1954 from Laval University Faculty of Medicine in Quebec. He served in the Canadian Army Medical Corps in Canada and Europe as a Captain from 1954 to 1959, and then located in Fort Kent where he now practices.

He is a member and Secretary of the Aroostook County Medical Society, a member of the Maine Medical Association, and the New Brunswick Medical Society. He has represented the 9th District on the M.M.A. Executive Committee since 1973.

Dr. Ouellette is married to the former Blanche Couillard and they have two children.

Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The bylaws of the Maine Medical Association were amended in June of 1973 as follows: Chapter I, Section 11, — "Each member of the Maine Medical Association shall be required to report his activities in continuing medical education every year according to a format provided by the Committee on Continuing Medical Education."

Only active, dues-paying members are required to report this year.

Please fill in your activity report promptly and return to the M.M.A. office, P.O. Box 250, Brunswick, Maine 04011.

Maine Medical Association

STANDING COMMITTEES — 1975-1976

Standing Committees for 1975-1976 as proposed by the Committee on Nominations and approved at the Second Meeting of the House of Delegates of the Maine Medical Association at Rockport, Maine, June 15, 1975.

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*As voted by the M.M.A. Executive Committee on 6/17/75, this entire committee is appointed for 1 year only.



Maine Blue Cross and Blue Shield News

YOU CAN GO HOME NOW

Maine Blue Cross and Blue Shield has been offering to pay physicians and other health care practitioners for care of a patient in his home since 1972. The home health care program offers an extensive range of benefits to subscribers. The fact that personal care and home environment supportive services, as well as medical services, are frequently needed for the care of individuals in their homes, presented a difficult challenge in the structuring of a cost effective program. The Coordinated Home Health Care Program as it is being offered here in Maine meets this challenge.

Home health care services refers to an extensive range of physician-directed professional, technical, and related medical and personal care services which are delivered to patients in their places of residence on a visiting basis.

Home care services are provided for the purpose of implementing a plan of treatment established for a patient's care and maintenance in his home.

The Blue Cross Coordinated Home Health Care program was established as a cost containment mechanism. It is offered to Blue Cross subscribers in lieu of hospitalization. Patients that would require more inpatient days are discharged with the doctor's permission to receive care in their homes. The intent is to free hospital beds for those patients which require more intensive care and to create dollar savings by paying for services rendered without the room and board costs.

Home health care services covered by the Blue Cross contract can include but are not limited to: nursing, physical therapy, respiratory therapy, speech therapy, occupational therapy, medical-social service, nutritional guidance, home health aide services, diagnostic (lab & x-ray) services, medical supplies and equipment, drugs, and ambulance services.

The Blue Shield participation in this project includes payment for the physician's visits for patient home care management, either a home or office visit.

A home care agency can be a valuable community resource for a physician practitioner. It can facilitate the availability of many services and provide him with support in the care of his home patient.

For more information about home care in your area, contact your Provider and Professional Relations Administrator at Maine Blue Cross and Blue Shield, 110 Free Street, Portland, Maine 04101.

The **ALLBEE with C** Scrapbook of Vitamin Facts & Fallacies



The Indian fruit-eating bat, almost all monkeys, man and the guinea pig are the only mammals whose bodies lack an enzyme needed to synthesize ascorbic acid from glucose! Hence they must obtain their vitamin C from exogenous sources

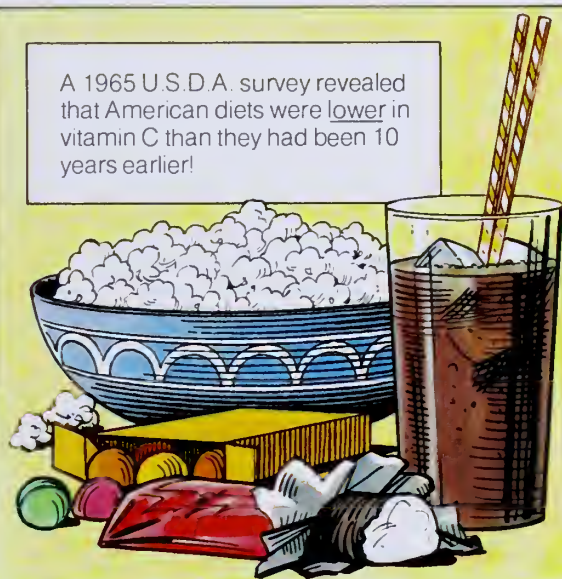


De Joinville writing about a 13th century crusade reported that barber surgeons had to "cut away the dead flesh from the gums to enable people to masticate their food." The disease he described was probably scurvy.



The outer leaves of cabbage and brussels sprouts contain more vitamin C than the heads. Yet, ironically, these are often trimmed away by the grocer to improve appearance and enhance sales appeal! Many housewives trim them even more before cooking!

A 1965 U.S.D.A. survey revealed that American diets were lower in vitamin C than they had been 10 years earlier!



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hyoscine hydrobromide	0.0065 mg.	0.0065 mg.	0.0195 mg
phenobarbital	($\frac{1}{4}$ gr.) 16.2 mg	($\frac{1}{2}$ gr.) 32.4 mg	($\frac{3}{4}$ gr.) 48.6 mg
(warning: may be habit forming)			

Brief summary. Adverse Reactions: Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Contraindications: Glaucoma; renal or hepatic disease; obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); or hypersensitivity to any of the ingredients.

A-H ROBINS A H Robins Company Richmond Virginia 23220



DEAN H. FISHER, M.D.
COMMISSIONER

State of Maine

Department of Health and Welfare

Recommendation of the Public Health Service Advisory Committee on Immunization Practices

Rabies Prophylaxis

INTRODUCTION

Although human rabies is rare in the United States, thousands of persons receive rabies prophylaxis each year. Management of those who possibly have been exposed to rabies infection is of paramount importance. The following is a current interpretation both of the risk of infection and the efficacy of treatment. It incorporates many basic concepts of the World Health Organization Expert Committee on Rabies.

The problem of whether or not to immunize those bitten, scratched, or otherwise exposed to rabies by animals suspected of being infectious is a perplexing one for physicians. All available methods of systemic treatment are complicated by instances of adverse reactions, a few of which have resulted in death or permanent disability. Furthermore, decisions on management must be made immediately, because the longer treatment is postponed, the less likely it is to be effective.

Data on the efficacy of active and passive immunization after rabies exposure have come principally from studies in animals. Because rabies has occasionally developed in humans who had received antirabies prophylaxis, the data have been questioned. Evidence from laboratory and field experience in many areas of the world, however, indicates that post-exposure prophylaxis is usually effective when appropriately used.

Rabies in the United States

Rabies in humans has decreased from an average of 22 cases per year in 1946-50 to only 1 or 2 cases per year since 1963. Rabies in domestic animals has

diminished similarly. In 1946, for example, there were more than 8,000 cases of rabies in dogs, compared with 230 in 1971. Thus, the likelihood of humans being exposed to rabies by domestic animals has decreased greatly; although bites by dogs and cats continue to be responsible for the overwhelming majority of antirabies treatments.

In contrast, the disease in wildlife — especially skunks, foxes, raccoons, and bats — has become increasingly prominent in recent years, accounting for more than 70 percent of all reported cases of animal rabies in 1971. Wild animals constitute the most important source of infection of man and domestic animals in the United States today. In 1971, only a single State reported no wildlife rabies.

Antirabies Treatment in the United States

More than 30,000 persons receive post-exposure antirabies treatment each year. However, there is no information on the number of persons actually exposed to rabid animals.

In the United States, nervous tissue origin rabies vaccine of the Semple type (NTV) was used almost exclusively until 1957, when duck embryo origin vaccine (DEV) was licensed. More than 90 percent of those who received rabies prophylaxis in the United States in 1971 were given DEV.

RABIES VACCINES

Duck Embryo Vaccine (DEV)

Prepared from embryonated duck eggs infected with a fixed virus and inactivated with beta-propiolactone.

Nervous Tissue Vaccine (NTV)

Prepared from rabbit brain infected with a fixed virus and inactivated with phenol (Semple type) or inactivated with ultraviolet irradiation.

Antigenicity of Vaccines

The antigenicity of NTV is often higher than that of DEV when tested in experimental animals. However, all lots of both vaccines must pass minimum potency tests established by the Division of Biologics Standards. There is evidence that the serum antibody response in humans is detectable sooner with DEV, but the eventual level of response is frequently higher with NTV.

Effectiveness of Vaccines in Humans

In the United States, comparative effectiveness of vaccines can be judged only by reported failures. During the years 1957 through 1971 when both vaccines were available, there were 6 rabies deaths among the 125,000 NTV-treated persons (1:20,800) and 12 among the 310,000 treated with DEV (1:25,800).

Reactions

Erythema, pruritus, pain, and tenderness at the site of inoculation are common with both DEV and NTV. Systemic responses, including low-grade fever or rarely shock, may occasionally occur late in the course of therapy with either vaccine, usually after 5-8 doses. In rare instances, serious reactions have occurred after the first dose of DEV or NTV, particularly in persons previously sensitized with vaccines containing avian or rabbit brain tissue.

Neuroparalytic reactions occur rarely with DEV. They much more frequently follow NTV, especially after repeated courses of treatment with this preparation.

Choice of Vaccine

Treatment-failure rates for the 2 vaccines are not significantly different; therefore, the lower incidence of central nervous system reactions with DEV makes it preferable to NTV.

RATIONALE OF TREATMENT

Every exposure to possible rabies infection must be individually evaluated.

In the United States, the following factors should be considered before specific antirabies treatment is initiated:

Species of Biting Animal

Carnivorous animals (especially skunks, foxes, coyotes, raccoons, dogs, and cats) and bats are more likely to be infective than other animals. Bites of rabbits, squirrels, chipmunks, rats, and mice, seldom, if ever, call for rabies prophylaxis.

Circumstances of Biting Incident

An UNPROVOKED attack is more likely to mean that the animal is rabid. (Bites during attempts to feed or handle an apparently healthy animal should generally be regarded as PROVOKED.)

Type of Exposure

Rabies is transmitted by inoculation of infectious saliva through the skin. Thus, the likelihood that rabies infection will result from exposure to a rabid animal varies with the nature and extent of the exposure. Two categories of exposure should be considered:

Bite wounds: any penetration of the skin by teeth.

Non-bite wounds: scratches, abrasions, or open wounds.

Vaccination Status of Biting Animal

A properly immunized animal has only a minimal chance of developing rabies and transmitting the virus.

Presence of Rabies in Region

If adequate laboratory and field records indicate that there is no rabies infection in a domestic species within a given region, local health officials are justified in considering this in recommendations on anti-rabies treatment following a bite by that particular species.

MANAGEMENT OF BITING ANIMALS

A healthy domestic dog or cat that bites a person should be captured, confined, and observed by a veterinarian for 10 days. (The commonly used 5-7 day observation period may not always be adequate.) Any illness in the animal should be reported immediately to the local health department.

If the dog or cat develops signs suggestive of rabies, the animal should be sacrificed and the head removed and shipped under refrigeration to a qualified laboratory designated by the local or State health department for examination.

Early signs of rabies in wild or stray animals cannot be interpreted reliably; therefore, any such animal that bites or scratches a person should be killed at once (without unnecessary damage to the head) and the brain examined for evidence of rabies.

If examination of the brain by fluorescent antibody technique is negative for rabies, the bitten person need not be treated.

LOCAL TREATMENT OF WOUNDS

Immediate and thorough local treatment of all bite wounds and scratches is perhaps the most effective means of preventing rabies. Experimentally, the incidence of rabies in animals can be markedly reduced by local therapy alone.

First-Aid Treatment to be Carried Out Immediately

Copious flushing with soap and water.

Treatment By or Under Direction of Physician

1. Thorough flushing and cleansing into the wound with soap solution. Quaternary ammonium

POST-EXPOSURE ANTIRABIES GUIDE

The following recommendations are only a guide. They should be used in conjunction with knowledge of the animal species involved, circumstances of the bite or other exposure, vaccination status of the animal, and presence of rabies in the region.

Animal and Its Condition		Treatment	
Species	Condition at Time of Attack	Kind of Exposure	
		Bite*	Non-Bite*
Wild Skunk Fox Raccoon Bat	Regard as Rabid	S + V ¹	S + V ¹
Domestic	Dog Healthy	None ²	None ²
	Escaped (unknown)	S + V	V ³
	Cat Rabid	S + V ¹	S + V ¹
Other		Consider individually - See "Rationale of Treatment"	

* See text definitions

V Rabies Vaccine

S Antirabies Serum

¹ Discontinue vaccine if fluorescent antibody (FA) tests of animal killed at time of attack are negative

² Begin S + V at first sign of rabies in biting dog or cat during holding period (10 days)

³ 14 Doses of DI V

compounds may also be used.*

2. If antirabies serum is indicated, (See Passive Immunization), up to one-half of the total dose should be thoroughly infiltrated around the wound. As in all instances when horse serum is to be used, a careful history should be taken and tests for hypersensitivity performed.

3. Tetanus prophylaxis and measures to control bacterial infection, as indicated.

POST-EXPOSURE PROPHYLAXIS

The following recommendations are intended only as a guide. They may be modified according to knowledge of the species of biting animal, circumstances surrounding the biting incident, vaccination status of the animal, and presence of rabies in the region.

Active Immunization

Vaccine without serum: 14 daily injections of the vaccine in the dose recommended by the manufacturer.

Vaccine with serum: When serum is used, 21 doses of vaccine are recommended. These may be given

*Such as Zephiran (Benzyl ammonium chloride). All traces of soap should be removed before applying quaternary ammonium compounds because soap neutralizes their activity.

as 21 daily doses or 14 doses in the first 7 days (either as 2 separate injections or a double dose), and then 7 daily doses. Two booster doses, the first 10 days and the second at least 20 days after completion of the primary course, are necessary to assure lasting protection.

Precautions: Vaccine should be given subcutaneously in the abdomen, lower back, or lateral aspect of thighs; rotation of sites is recommended. Local reactions are common and do not contraindicate continuing treatment.

When rabies vaccine must be given to a person with a history of hypersensitivity, especially to avian or rabbit tissues, antihistaminic drugs may be given. Epinephrine is indicated in reactions of the anaphylactoid type. If serious allergic manifestations preclude continuation of prophylaxis with one vaccine, the other may be used.

If meningal or neuromyolytic reactions develop, vaccine treatment should be discontinued altogether. Corticosteroids may interfere with development of active immunity and should only be used to treat neuromyolytic reactions.

Passive Immunization

Hyperimmune serum has proved effective in

preventing rabies. Its use in combination with vaccine is considered the best post exposure prophylaxis. Human hyperimmune rabies immune globulin is now available and is the treatment of choice when serum therapy is required. Because horse serum has induced serum sickness in at least 20 percent of those who have received it, it should be used only when indicated. Horse serum may be indicated when unusual delays would occur in obtaining the human immune globulin.*

Hyperimmune serum is recommended for ALL BITES by animals in which rabies cannot be excluded and for non-bite exposure to animals proven or suspect to be rabid (see accompanying guide). When indicated, antirabies serum should be used regardless of the interval between exposure and treatment.

The recommended dose of equine antirabies serum is 40 IU/kg, i.e., approximately 20 IU/lb or 1000 IU (1 vial)/55 pounds. Up to 50 percent of the antiserum should be used to infiltrate the wound and the rest administered intramuscularly. As previously noted, when using serum, a careful history must be obtained and appropriate tests for hypersensitivity performed.

PRE-EXPOSURE PROPHYLAXIS

The relatively low frequency of reactions to DEV has made it practical to offer pre-exposure immunization to persons in high-risk groups: veterinarians, animal handlers, certain laboratory workers, and individuals, especially children, living in areas of the world where rabies is a constant threat. Others whose vocational or avocational pursuits result in frequent contact with dogs, cats, foxes, skunks, or bats should also be considered for pre-exposure prophylaxis.

Two 1.0 ml injections of DEV given subcutaneously in the deltoid area 1 month apart should be followed by a third dose 6-7 months after the second dose. This series of 3 injections can be expected to produce neutralizing antibody in 80-90 percent of vaccines by 1 month after the third dose.

For more rapid immunization, 3 injections of DEV, 1.0 ml each, should be given at weekly intervals with a fourth dose 3 months later. This schedule elicits an antibody response in about 80 percent of

the vaccinees.

All who receive the pre-exposure vaccination should have serum tested for neutralizing antibody 3-4 weeks after the last injection. Tests for rabies antibody can be arranged by State health department laboratories. If no antibody is detected, booster doses should be given until a response is demonstrated. Persons with continuing exposure should receive 1.0 ml boosters every 2-3 years.

When an immunized person with previously demonstrated rabies antibody is bitten by a rabid animal, it is suggested that he receive 5 daily doses of vaccine plus a booster dose 20 days later. Antirabies serum is not necessary in this case and, in fact, might inhibit a rapid anamnestic response. For non-bite exposures, an immunized person with antibody needs only a single dose of vaccine. If it is not known whether an exposed person ever had antibody, the complete post-exposure antirabies treatment should be given.

ACCIDENTAL INOCULATIONS WITH LIVE RABIES VIRUS VACCINE

Persons inadvertently inoculated with the Flury strain vaccine are not considered at risk, and antirabies prophylaxis is not indicated. No information is available by which to judge risk from accidental inoculation of other attenuated strains in veterinary use.

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*Note: This paragraph has been revised from the original by the Maine State Department of Health and Welfare.

County Society Notes

Cumberland

The annual meeting of the Cumberland County Medical Society was held on May 15, 1975 at the Red Coach Grill. There were 89 members present.

A motion to omit the reading of the minutes was seconded and approved. The treasurer's report was accepted.

A letter from the Secretary of the Department of Health and Welfare concerning the acceptance of a PSRO organization was read.

Reports from committees on Medical Careers, Medical Legal Liaison, Malpractice, Utilization Review, Professional Ethics, Health Insurance and Peer Review were accepted.

A resolution of the death of Dr. William Casey was spread upon the records of the Society.

Following this, the report of the Nominating Committee was presented. The subsequent balloting produced these results:

President: Dr. Robert E. McAfee, Portland

Vice-President: Dr. Walter B. Goldfarb, Portland

Secretary-Treasurer: Dr. Wesley J. English, Portland

Professional Ethics Committee: Dr. Alphonse Telfeian, Portland

Executive Committee: Dr. Philip G. Whitney, Portland

Delegates to the M.M.A. House of Delegates: Drs. Robert

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McGuire, David L. Adams, Thomas M. Ashby, Donald P.

Cole, Bernard Givertz, Walter B. Goldfarb, William L.

MacVane, Jr. and Stephen E. Monaghan, all of Portland;

Frederick S. Larned, Cape Elizabeth; and Robert H. Pawle,

Falmouth. Alternates: Drs. Louis A. Ciampi, Patrick A.

Dowling, Andrew P. Iverson, Jr., John D. Kilgallen,

Thomas A. Martin, Jr., Irving J. Poliner, William J. Hall,

III, John E. Knowles, Bruce D. Nelson and Stanley B.

Sylvester, all of Portland; Martin A. Barron, Jr. and Theodore

J. Hallee, both of Cape Elizabeth; and Alfred E. Swett,

North Windham.

Dr. Douglas R. Hill presented President Stan Sylvester with a complimentary gavel and thanked him for his many years of service to the Society.

Dr. Sylvester introduced our guest speaker, Dr. John B. Madigan, President of the Maine Medical Association, who presented many timely and interesting ideas.

A motion to endorse the Telmed program presented by Dr. Michael Taylor was passed.

Dr. Douglas R. Hill then presented the Maine Medical Association budget for next year which would permit expansion of the Society's functions. He also explained the need for a proposed increase in the State dues. A motion to instruct the delegates to support these proposals at the annual House of Delegates Meeting in June was passed.

Dr. Wesley J. English presented more information concerning a screening clinic in Freeport. Following lengthy discussion, the program was accepted as presented.

Dr. Benjamin Zolov expressed concern over the scheduling of the Maine Medical Association meeting at the same time as the American Medical Association. Many members echoed the same feelings.

Dr. Thomas A. Martin, Sr. indicated the urgent need for a ball game-beer party event in the near future.

Dr. Stephen E. Monaghan will introduce a motion to change the meetings of the delegates from weekends to weekdays at the June meeting in Rockport.

There being no further business to transact, the meeting was adjourned at 10:15 p.m.

ALFRED E. SWETT, M.D., *Secretary*

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Health Care Delivery in Maine II: Conditions Explaining Hospital Admission

JOHN E. WENNBURG, M.D.* ALAN GITTELSON, Ph.D.** and DAVID SOULE†

The incidence of surgery has been shown to vary extensively among Hospital Service Areas in Maine,¹ a finding consistent with previous studies of patterns of use of surgery among neighboring communities.²⁻⁶ In the present study, our purpose is to examine the incidence of hospitalization and bed use according to the conditions explaining hospital admission and to consider the significance of our findings for hospital facility planning. Data are presented comparing hospitalization rates among the populations of the five Maine Comprehensive Health Planning Regions and among their constituent Hospital Service Areas (HSAs). The differences among Planning Regions in hospital use for treating patients with conditions belonging to 13 major International Classification of Disease (ICDA) groups are studied. For patients with diseases of the respiratory system, we show the specific conditions assigned as the cause of hospital admission.

Our results show little difference among Planning Regions in use of hospital for patients with congenital anomalies and for conditions associated with pregnancy. However, for illnesses of the respiratory tract, for infectious and parasitic illnesses and for ill defined conditions or symptoms, the range of differences among the Planning Regions in use of hospitals is greater than two-fold. For several common, nonsurgical illnesses of the respiratory

tract, the range in incidence rates is more than five-fold, a variability greater than that for tonsillectomy. The variety of use of hospitals for many common medical and surgical conditions indicates the importance of taking population-based data on patient mix into account in interpreting the need of communities for expansion of their bed supply.

METHODS

The methods of measuring per capita use of hospital care are presented in the first article of this series.¹ A discharge abstract for each patient admitted to any Maine hospital in 1973 provides information on diagnoses, procedures and patient characteristics, including town of residence. Utilization rates are computed for HSAs, which are groups of adjacent Maine towns around given facilities, and for the five Maine Comprehensive Health Planning Regions based on total residential use of health services, irrespective of whether care was obtained in or out of the local area or planning region. The latter include the Southern Maine, Tri-County, Kennebec Valley, Northeast, and Aroostook regions. The locations of the five Maine Comprehensive Health Planning Regions and 42 Maine Hospital Service Areas are shown in Figure 1. Appendix Table 1 lists, for each Comprehensive Health Planning Region, the populations and number of hospital beds of its constituent HSAs.

The condition causing hospitalization is entered on the discharge abstract as the "principal diagnosis" and is defined as "the condition, determined after study, that occasioned the patient's admission to the hospital."⁷ The frequencies of use by all Maine hospitals of each of 13 major ICDA groups are presented in Appendix Table 2. Diseases of

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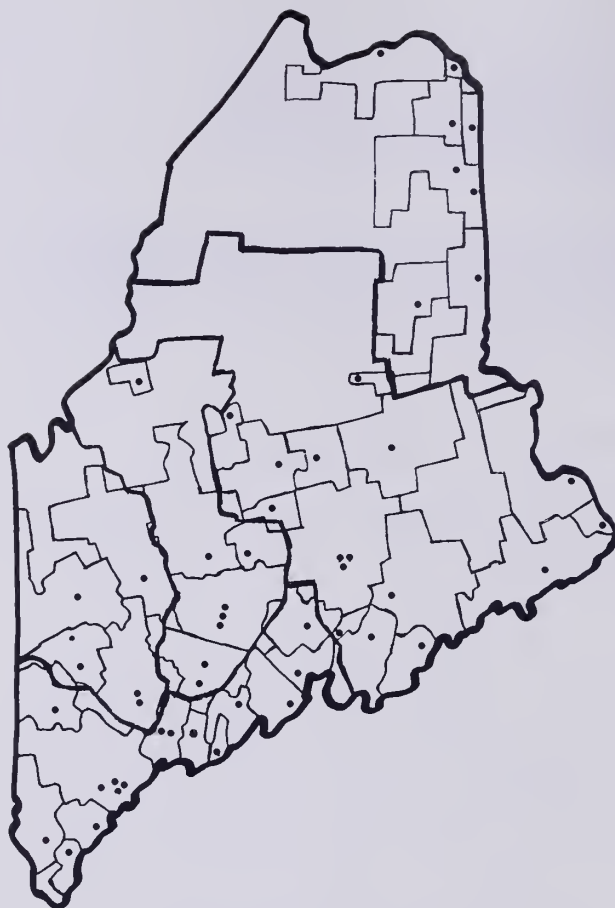


Figure 1. Showing the 5 Maine Comprehensive Health Planning Regions and the 42 Hospital Service Areas.

the respiratory system are examined in more detail in Appendix Table 3. Twelve groups of respiratory conditions are based on the acute or chronic nature of the condition, the site of the illness within the respiratory tract and diagnostic specificity. The ICDA codes within each subgroup of respiratory conditions and their frequency of use are presented below.

We measure the average daily number of beds occupied by patients per 1000 population by dividing the patient rate by 365. The patient day rate is the number of days the residents of an area spend in the hospital annually per 1000 persons at risk. Among the areas, the average number of beds occupied by the population is studied for the same groupings of ICDA codes used in the study of incidence of causes of hospitalization. The incidence and patient day rates used in the study have been age adjusted to the total Maine population to reduce the effect of population differences in age structure as a contributor to differences among areas. For the types of utilization rates studied, a number of areas are significantly higher or lower than the State average by chi square tests. Of greater interest is the extent to which areas differ which we indicate by

APPENDIX TABLE 1

<i>Regions and Areas</i>	<i>1970 Population</i>	<i>Number of Beds (1973)</i>
Comprehensive Health Planning Regions		
Southern Maine Comprehensive Health Planning Region	362848	1665
Hospital Service Areas		
Bath	16578	92
Belfast	12399	58
Biddeford	47603	135
Boothbay Harbor	5156	36
Bridgton	8922	34
Brunswick ¹	30702	134
Camden	5491	33
Damariscotta	6029	42
Portland ³	170879	893
Rockland ¹	28043	87
Sanford	20908	82
York	10138	39
Tri-County Comprehensive Health Planning Region	153099	690
Hospital Service Areas		
Farmington	21345	49
Lewiston ¹	95551	503
Norway	10986	41
Rumford	25217	97
Kennebec Valley Comprehensive Health Planning Region	149112	757
Hospital Service Areas		
Augusta-Gardiner ¹	61146	225
Jackman	1151	8
Pittsfield	11298	31
Skowhegan	23877	92
Waterville ²	51640	401
Northeast Comprehensive Health Planning Region	206799	945
Hospital Service Areas		
Bangor ²	104591	494
Bar Harbor	8708	67
Blue Hill	7172	24
Calais	9848	71
Castine	1080	16
Dexter	6981	19
Dover-Foxcroft	8638	32
Eastport	2867	14
Ellsworth	13043	64
Greenville	2763	24
Lincoln	11525	30
Machias	13358	38
Millinocket	11977	34
Milo	4248	18
Aroostook Comprehensive Health Planning Region	87201	472
Hospital Service Areas		
Caribou	12716	73
Fort Fairfield	5552	65
Fort Kent	19442	70
Houlton	15793	119
Island Falls	4399	21
Presque Isle ¹	24816	94
Van Buren	4483	30

¹HSA contains 2 hospitals

²HSA contains 3 hospitals

³HSA contains 4 hospitals

APPENDIX TABLE 2

FREQUENCY OF CONDITIONS CAUSING HOSPITALIZATION, GROUPED
MAJOR SYSTEMS OF DISEASE; ALL MAINE HOSPITALS 1973

Diagnosis Group	ICDA-8	Number of Total Discharges	Percent of All Discharges
Digestive System	520-577	20383	12.97
Respiratory System	460-519	19893	12.66
Circulatory System	390-458	19192	12.21
Pregnancy, Delivery, and Puerperium	630-678	17932	11.07
Genitourinary System	580-629	15913	10.13
Accidents, Injuries, and Violence	800-999	15689	9.98
Nervous	290-389	11698	7.44
Neoplasm	140-239	10275	6.54
Skin and Subcutaneous Tissue	680-738	8986	5.72
Symptoms and Ill-Defined Conditions	780-796	7213	4.59
Endocrine, Nutritional, and Metabolic	240-289	4327	2.75
Infective and Parasitic	000-136	4294	2.73
Congenital Abnormalities	740-779	1838	1.17
All Conditions	000-999	157085	100.00

the coefficient of variation. It is obtained by dividing the standard deviation of the rates over areas by the mean and expressing the ratio as a percent. The coefficient provides an index of variability in the observed rates. The range between highest and lowest rates also is used as a measure of variability.

RESULTS

Variations in Incidence of Hospitalization Among and Within Planning Regions. Substantial differences exist in the incidence of hospitalization among the Planning Regions (Table 1). In the Aroostook and Kennebec regions, discharged are 23% and 21% higher than the State average while the Southern Maine, Northeast and Tri-County regions have rates lower than the State average by 8%, 7%, and 3% respectively. Comparing the highest and the lowest Comprehensive Health Planning Regions, 35% more discharges per capita occurred in the Aroostook Planning Region in 1973 than in the Southern Maine Planning Region. For the Hospital Service Areas within the five Planning Regions, the rates of hospitalization show greater variation than between the Planning Regions themselves (Table 1). The smallest range of difference is 1.43 fold in the Tri-County region; the largest is 1.96 fold in the Northeast Planning Region. While the coefficient of variation among Planning Regions is 15.6%, the intra-regional coefficients range from 15% to 22%.

The results indicate that differences in hospitalization practices within the HSAs of a Planning Region are greater than those among the regions themselves. Population size for the area and differences among HSAs in rate of use of hospitals located outside of Maine may contribute to greater variation among HSAs than among the larger regions, but we believe these effects are not the major reason for the observed differences. The effect of small population size has been reduced by excluding

areas with less than 4,000 residents from the analysis. Based on State average rates, the expected number of cases in the smallest HSA is 775. None of the lowest ranked HSAs are located on the New Hampshire border.

Incidence of Hospitalization by Major ICDA Group. The variability in use of hospitals is not similar for all conditions (Table 2). The greatest variability is among persons admitted for conditions related to the respiratory tract, for infective and parasitic diseases and for ill-defined conditions where the rates among Planning Regions show over a two-fold range of differences. By contrast, admissions for conditions associated with pregnancy and for congenital anomalies show the least variability; the highest rate is only 25% and 18% greater than the lowest, respectively. It is of note that conditions that vary least are defined by specific, well agreed upon criteria.

Incidence of Hospitalization for Specific Respiratory Conditions. Age-adjusted rates of use of hospitals for the major ICDA group of respiratory diseases show greater than a two-fold range of difference among Planning Regions. Specificity concerning the patient mix which contribute to these differences in rates is obtained by examining use of each individual ICDA code (Appendix Table 3). About 45% of respiratory admissions are for acute infections of the respiratory tract, 32% for hypertrophy of the tonsil, and 11% for chronic lung conditions. A group of less common conditions make up the remaining 12% of cases. Table 3 shows how the Planning Regions differ with respect to use of hospitals for acute and chronic respiratory tract conditions and for tonsillectomy. For hypertrophy of the tonsils, the Kennebec region exceeds the lowest area by 207%. For acute infections, the highest region is Aroostook which exceeds Kennebec by 32% and Southern Maine by 268%. Upper respiratory infections contribute most to the dif-

APPENDIX TABLE 3

FREQUENCY OF USE OF INTERNATIONAL CLASSIFICATION DISEASE CODES FOR RESPIRATORY DISEASE MAINE HOSPITALS, 1973			
<i>ICDA Number</i>	<i>Number of Cases</i>	<i>Percent of All Respiratory Cases</i>	<i>Disease Label</i>
460	103	0.50	Common Cold
461	46	0.22	Acute Sinusitis
462	362	1.75	Acute Pharyngitis
463	383	1.85	Acute Tonsillitis
464	409	1.98	Acute Laryngitis
465	878	4.25	Acute Respiratory Infection, Unspecified
466	1,835	8.89	Acute Bronchitis
470	635	3.07	Influenza, Unqualified
471	45	0.22	Influenza with Pneumonia
472	145	0.70	Influenza, Other Respiratory Cold
473	45	0.22	Influenza with Digestive Manifestations
474	4	0.02	Influenza with Nervous Manifestations
480	215	1.04	Viral Pneumonia
481	334	1.62	Pneumococcal Pneumonia
482	97	0.47	Other Bacterial Pneumonia
483	39	0.19	Pneumonia from Other Specified Organism
484	28	0.14	Interstitial Pneumonia
485	947	4.59	Bronchopneumonia
486	2,178	10.55	Unspecified Pneumonia
490	652	3.16	Bronchitis, Unqualified
491	424	2.05	Chronic Bronchitis
492	1,144	5.54	Emphysema
492	764	3.70	Asthma
493	6,570	31.81	Hypertrophy of Tonsils
501	67	0.32	Peritonsillar Abscess
502	17	0.08	Chronic Pharyngitis
503	185	0.90	Chronic Sinusitis
504	496	2.40	Deviated Nasal Septum
505	132	0.64	Nasal Polyp
506	65	0.31	Chronic Laryngitis
507	21	0.10	Hay Fever
508	344	1.67	Other Disease of Upper Respiratory Tract
510	32	0.15	Empyema
511	127	0.61	Pleurisy
512	142	0.69	Spontaneous Pneumothorax
513	19	0.09	Lung Abscess
514	77	0.37	Pulmonary Congestion
515	4	0.02	Pneumoconiosis
516	1	—	Other Pneumoconiosis
517	83	0.40	Chronic Interstitial Pneumonia
518	69	0.33	Bronchiectasis
519	487	2.36	Other Diseases of Respiratory System
450-519	20,650		

TABLE 1

AGE-ADJUSTED DISCHARGES FROM HOSPITAL PER 1000 POPULATION, MAINE COMPREHENSIVE HEALTH PLANNING REGIONS AND CONSTITUENT HOSPITAL SERVICE AREAS (1973)					
	<i>Southern Maine</i>	<i>Tri-County</i>	<i>Kennebec</i>	<i>Northeast</i>	<i>Aroostook</i>
Region as a Whole	150	157	197	152	204
Hospital Service Areas Ranked within Regions:					
Highest	212	192	235	249	309
2nd Highest	193	158	234	230	283
2nd Lowest	127	153	204	146	185
Lowest	117	134	157	127	172
Ratio of highest to lowest ranked					
Hospital Service Areas	1.81	1.43	1.50	1.96	1.80
Coefficient of variation*	18%	15%	18%	21%	22%

*The coefficient of variation includes all HSAs within a planning region except those with populations less than 4,000.

TABLE 2

**AGE-ADJUSTED DISCHARGE RATE BY CONDITIONS CAUSING HOSPITALIZATION IN FIVE MAINE
COMPREHENSIVE HEALTH PLANNING REGIONS, RATES PER 10,000 POPULATION, 1973**

<i>Condition*</i>	<i>Southern Maine</i>	<i>Tri-County</i>	<i>Kennebec</i>	<i>Northeast</i>	<i>Aroostook</i>	<i>Ratio of highest to lowest</i>	<i>Coefficient of Variation</i>
Infective and Parasitic	31	49	64	40	75	2.42	34.6
Neoplasm	112	114	116	88	106	1.32	10.3
Endocrine	41	50	61	35	50	1.74	21.3
Nervous	116	108	131	101	143	1.42	14.3
Circulatory	181	191	228	187	296	1.64	22.1
Respiratory	151	183	300	199	340	2.25	34.5
Digestive	190	202	256	206	271	1.43	16.0
Genitourinary	182	155	159	145	182	1.26	10.4
Delivery	191	193	197	182	158	1.25	8.7
Skin and Subcutaneous Tissue	81	82	122	92	126	1.56	22.2
Congenital	19	17	20	20	20	1.18	6.3
Ill-defined	58	80	117	67	86	2.02	28.0
Injuries	150	151	204	158	188	1.36	14.1
All Conditions	1504	1573	1975	1520	2035	1.35	15.2

*ICDA codes for each group are shown in Appendix Table 2.

TABLE 3

**CONDITIONS CAUSING HOSPITALIZATION OF RESIDENTS WITH RESPIRATORY
ILLNESS IN FIVE MAINE COMPREHENSIVE HEALTH PLANNING REGIONS, 1973**

<i>Condition</i>	<i>ICDA Code</i>	<i>Percent of All Respiratory Cases</i>	<i>Rates per 10,000 Population Southern Maine Rate</i>	<i>Tri- County Rate</i>	<i>Kenne- bec Rate</i>	<i>North- east Rate</i>	<i>Aroos- took Rate</i>	<i>Ratio of Highest to Lowest</i>	<i>Coef- ficient of Variation</i>
Acute Upper Respiratory Tract Condition and the Common Cold	460,465	4.8	5.2	6.1	15.0	6.7	29.7	5.71	82.7
Acute Sinusitis, Pharyngitis, Tonsillitis, Laryngitis	461-464	5.8	7.1	9.5	15.1	9.5	30.1	4.23	65.4
Acute Bronchitis	466	8.9	16.0	12.3	39.0	12.4	29.1	3.17	54.4
Influenza with or without Complication	470-474	4.2	3.8	5.8	12.7	9.0	26.2	6.89	77.2
Pneumonia, Viral or Bacterial or Interstitial	480-484	3.5	11.3	4.4	8.6	8.7	8.7	2.57	29.7
Bronchopneumonia, unspecified	485	4.6	6.4	8.8	8.9	10.2	16.3	2.55	36.7
Pneumonia unspecified, or Bronchitis, unqualified	486,490	13.7	20.9	31.1	33.0	32.6	33.8	1.62	17.6
Chronic Bronchitis, Emphysema	491-492	7.6	14.9	15.9	18.4	13.9	19.9	1.43	15.0
Asthma	493	3.7	6.7	4.8	9.1	7.2	12.1	2.52	34.7
Hypertrophy of Tonsils	500	31.8	49.8	64.4	103.0	66.0	80.7	2.07	27.7
Deflected Nasal Septum	504	2.4	6.4	3.1	5.1	2.9	9.4	3.24	49.7
All Others	501-504								
	506-519	9.1	15.0	17.2	28.7	17.1	23.6	1.91	28.0

ferences in use of hospitals. Influenza admissions are nearly 7 times more common; acute upper respiratory conditions are 5.7% and acute infections of the naso-pharynx are 4.2 times more common in Aroostook Planning Region than in the Southern Maine Planning Region. For pneumonia and bronchitis, hospitalizations are 1.6 to 2.5 times more common in Aroostook Planning Region except for pneumonias in which the etiologic agent or syndrome has been identified.

Use of Hospital Beds. We have measured the differences in use of hospital beds associated with variations in patient mix treated in Maine hospitals. Table 4 shows the average number of beds occupied

per 1000 population in each of the five Planning Regions and in the high and low bed use HSAs within Planning Regions. Among the Planning Regions, the population in the region of highest utilization used 35% more beds than the population of the lowest region. Within Planning Regions, differences among HSAs in use of hospital beds is considerably greater. The greatest differences are within the Northeast region where the range in bed use patterns is from 2.4 to 4.6 beds per 1000, a 1.9 fold difference.

The variability in use of beds is not the same for each major diagnostic grouping, and the degree of variability follows closely with differences among

TABLE 4

AVERAGE NUMBER OF BEDS OCCUPIED PER 1000 POPULATION, AGE-ADJUSTED RATES FOR FIVE MAINE COMPREHENSIVE HEALTH PLANNING REGIONS AND CONSTITUENT HOSPITAL SERVICE AREAS (1973)					
	<i>Southern Maine</i>	<i>Tri-County</i>	<i>Kennebec</i>	<i>Northeast</i>	<i>Aroostook</i>
Region as a Whole	2.9	3.3	3.7	2.8	3.9
<i>Hospital Service Areas Ranked within Regions:</i>					
Highest	3.6	3.6	4.6	4.6	5.5
2nd Highest	3.5	3.4	4.3	4.0	4.9
2nd Lowest	2.1	2.9	4.0	2.6	3.4
Lowest	2.0	2.3	2.8	2.4	3.4
Ratio of highest to lowest ranked Hospital Service Areas	1.80	1.57	1.64	1.92	1.62
Coefficient of Variation*	20%	19%	20%	21%	20%

*The coefficient of variation includes all HSAs within a planning region except those with populations less than 4,000.

the areas in the incidence of hospitalization. (Table 5). The pattern of bed use among the regions are quite similar for conditions which have similar rates of hospitalization. For congenital anomalies, and deliveries, bed-use ranges from 2.0 to 2.4 beds per 10,000 population, a 1.2 fold difference. On the other hand, for conditions with greater variability in incidence, respiratory, infective and parasitic diseases and the class of conditions labeled as "ill defined and symptoms," bed-use ranges from 3.6 beds per 10,000 in Southern Maine region to 7.8 beds per 10,000 in the Aroostook region, a 2.17 fold difference. The conditions with intermediate variability in incidence have intermediate variability in bed use. Again, to ascertain the specific reasons for differences among the regions, it is necessary to look more precisely at the conditions causing admission (Table 6). For example, in 1973, on an age-adjusted basis, for persons living in the Aroostook region, 1.4 beds per 10,000 were used for acute upper respiratory disease (excluding hypertrophy of the tonsils) and the flu; for persons living in Southern Maine, only 0.2 beds per 10,000 were used to treat these conditions. This represents a 7.7 fold difference in allocation of hospital facilities for these conditions.

DISCUSSION

While variations in incidence of common surgical procedures have been documented among regions and HSAs in Maine, Vermont and Kansas, we are aware of no previous report of use of hospitals in such areas according to the reasons for which the patients are admitted to the hospital. Our results indicate the importance of taking into account the case mix admitted to hospital on a per capita basis among neighboring areas in evaluating the uses made of hospitals. The overall incidence of hospitalization varies as much as 35% among the Plan-

ning Regions; however, certain classes of diseases contribute substantially more to the differences than do others. Admissions associated with pregnancy, and congenital anomalies, show the least differences among areas; infective and parasitic diseases, ill defined conditions and symptoms and respiratory diseases show the greatest. Medical as well as surgical conditions contribute to variation in hospitalization.

Studies in Vermont have shown that the volume of surgical procedures relate to differences in the specialty of active physicians and in the quantity of beds available in an area and not to differences in illness rates or access to physicians.⁸ Systematic studies of the relationship between health care system variables, the incidence of illness and rates of hospitalization for specific conditions causing admission are not available. Circumstantial evidence, however, suggest the differences relate to supply characteristics. In this study, the possible contribution of age-structure differences have been removed by age adjustment. It seems unlikely that the natural incidence of influenza, upper respiratory tract infections and hypertrophy of the tonsils will vary so as to account for the greater than five-fold differences we observed in rates of hospitalization for these conditions. Further, among the different, neighboring HSAs within a Planning Region — where differences among the populations-at-risk would seem less than when comparisons are based on Planning Regions — the use of hospitals varies more than between Planning Regions. The reason for this, we suggest, is because within a given HSA, usually one and at the most four hospitals are the principal institution involved, and there is thus a close correspondence between the medical community of an area and local rates of service. Within these areas, a relatively small cohort of physicians are the dominant

TABLE 5

AGE-ADJUSTED AVERAGE NUMBER OF BEDS OCCUPIED PER 100,000 POPULATION IN MAINE
COMPREHENSIVE HEALTH PLANNING REGIONS BY CONDITION CAUSING ADMISSION

Condition Ranked by Variability of Incidence Rates

<i>Condition</i>	<i>Southern Maine</i>	<i>Tri- County</i>	<i>Kennebec</i>	<i>Northeast</i>	<i>Aroostook</i>	<i>Ratio of Highest to Lowest</i>	<i>Coefficient of Variation</i>
Congenital	3.6	3.8	3.9	3.5	4.0	1.14	5.5
Delivery	19.9	18.1	19.6	18.3	15.9	1.25	8.6
Genitourinary	25.0	26.8	26.6	23.5	30.3	1.29	9.6
Nervous	20.4	22.2	24.4	17.9	22.0	1.36	11.3
Neoplasms	29.5	35.7	33.1	26.3	29.9	1.36	11.7
Digestive	38.2	46.7	48.0	40.6	52.5	1.37	12.8
Injuries	33.0	33.1	42.7	30.1	38.1	1.42	14.1
Circulatory	55.2	61.6	66.3	50.8	79.1	1.56	17.5
Skin and Subcutaneous Tissue	17.7	17.8	26.6	19.8	24.3	1.50	18.9
Endocrine	9.4	12.7	12.6	7.9	11.3	1.61	19.4
Ill-Defined	8.5	13.2	17.9	9.3	11.8	2.12	30.7
Infective and Parasitic	5.1	8.0	9.3	6.4	12.9	2.53	36.0
Respiratory	22.0	26.7	40.5	27.9	53.0	2.41	37.1

TABLE 6

AGE-ADJUSTED AVERAGE NUMBER OF BEDS OCCUPIED PER 100,000 POPULATION OF MAINE
COMPREHENSIVE HEALTH PLANNING REGIONS BY RESPIRATORY CONDITION CAUSING ADMISSION

Condition Ranked by Variability of Incidence Rates

<i>Condition</i>	<i>Southern Maine</i>	<i>Tri- County</i>	<i>Kennebec</i>	<i>Northeast</i>	<i>Aroostook</i>	<i>Ratio of Highest to Lowest</i>
Acute Upper Respiratory Tract Infection and Influenza	1.8	2.7	5.5	3.1	14.0	7.8
Acute Bronchitis and Pneumonias	9.3	11.1	17.6	12.3	19.6	2.1
Asthma, Chronic Bronchitis and Emphysema	5.0	5.0	6.4	5.2	7.7	1.5
Hypertrophy of Tonsils	2.9	3.6	6.2	3.8	5.3	2.1
All others	3.0	4.3	4.9	3.7	5.8	1.9

suppliers of medical services and local strategies for allocating hospitalized health care reflect in population-based rate profiles. Individual differences among physicians and facilities are more apparent under this geographic configuration than when HSAs are aggregated into larger Planning Regions.

Our observations on the variability in use of hospitals among neighboring areas have implications for facility planning. Under new Federal legislation, the states are required to establish programs to certify the need for facility construction, renovation and other changes in service in building programs that exceed \$100,000. Hospitals which do not comply with this requirement prior to undertaking construction face a cutoff of their eligibility to receive reimbursements under the Medicaid and Medicare programs. The model of "need" which planners commonly use in assessing building projects is based on the assumption that need for institutionalization is dependent largely on the natural incidence of illness. The planning issue is often interpreted as an assurance that beds are available for the next occasion when need arises, a perception that leads to a particular emphasis on improving the

efficiency of hospital operations as measured by length of stay and average daily census (percent of occupancy).

Our epidemiologic study of the incidence of hospitalization shows the importance of taking the surgical and medical patient mix into account in evaluating the need for facilities. While the relatively low variability in use of facilities for congenital anomalies, pregnancy associated conditions and neoplasms supports the belief that demand for hospitalization may be closely related to the natural incidence of the condition — and therefore accurately predicted by a model of hospital demand based on random incidence of medical conditions — hospitalization for these events represents only 18% of hospital use in Maine. The remaining causes of admission show considerably greater variability which cannot be accounted for by a demand model which postulates approximately similar rates of incidence among the regions and HSAs and consensus among the medical profession on need for hospitalization.

CONCLUSIONS

For many illnesses, the need for hospital beds

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Vasodilator Drugs in Peripheral Vascular Disease

JAY D. COFFMAN, M.D.

Pharmacological agents which produce an increase in blood flow by direct or indirect action on the peripheral blood vessels are collectively termed "vasodilators." These drugs are numerous, and all have been shown to increase blood flow to the limbs or various organs in normal animals. The animal studies have usually been the basis for their use in patients with peripheral vascular disease, although some agents have been documented to increase blood flow to the extremities in normal humans. No substantial evidence indicates that they induce the growth of new blood vessels. Whether these agents increase blood flow in the diseased states for which they are advertised is questionable. Since at least four to five million dollars a month is spent by patients in the United States to purchase these drugs, assessment of their clinical efficacy is extremely important both medically and economically.

Two types of vasodilator drugs might be useful in clinical practice: those which directly dilate blood vessels and those which are spasmolytic. In vasospastic diseases, symptoms are secondary to a reduced cutaneous blood flow; muscle blood flow is not usually of major concern. Drugs that dilate blood vessels of the skin by direct action and agents that induce vascular muscle relaxation by inhibiting normal or excessive sympathetic vascular tone should be of value.

In obstructive arterial disease, the problems are more complex. Distal to a stenosed or obstructed blood vessel, blood flow depends on the collateral blood vessels. Due to the resistance to flow in the small caliber collateral vasculature, the arterial

pressure distal to the obstructing lesion is decreased. During exercise, this pressure falls even lower, due to vasodilation induced by the accumulation of metabolites. The tension of the contracting muscle then exceeds the low arterial pressure distal to the obstruction and markedly decreases or even stops blood flow.¹ Patients with intermittent claudication, the most common symptom of obstructive arterial disease, usually have a resting muscle blood flow in the normal range. Dilating the vessels distal to the obstruction may not increase blood flow, especially if the resistance of the collateral vessels remains fixed. An ideal drug would dilate the collateral vessels or stimulate the growth of new vessels in order to raise the blood pressure below the obstruction. Vasodilator drugs must not lower systemic blood pressure; this has been shown to increase collateral vascular resistance. In fact, raising the systemic pressure is one of the most effective means of increasing collateral blood flow.²

The ideal vasodilator would increase blood flow in the ischemic, but not the normal, areas of the body; none of the presently available agents possess this property except when administered locally (intra-arterially). Even intra-arterial administration of vasodilator drugs may be detrimental if blood flow is adversely redistributed, i.e., muscle blood flow should not be increased at the expense of a decrease in cutaneous circulation. Vasodilator drugs do not always produce a fall in systemic blood pressure at rest but may during exercise with the additional vasodilatation in active muscles. This is especially characteristic of drugs affecting the sympathetic nervous system. The decrease in blood pressure would decrease flow to an ischemic limb. In some patients, vasodilatation in other areas of the body without obstructed arteries may actually "steal" flow from the affected limb. Since the vascular resistance would be much smaller in a vasodilated normal limb than in a limb supplied by small collateral vessels, blood flow would follow the path of least resistance to the normal limb.

Vasodilator drugs may be grouped according to their mode of action (Table 1). Direct acting drugs relax vascular smooth muscle and thereby affect both cutaneous and muscle blood vessels. Beta

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TABLE 1

PERIPHERAL VASODILATORS

Generic Name	Trade Name(s)	Range of Usual Daily Doses	Oral Dosage Sizes Available (mg)	Wholesale Cost per 100 dose units ^c
<i>Direct Acting Drugs</i>				
Isoxsuprine hydrochloride	Vasodilan	30 to 60 mg	10 20	6.43 11.94
Papaverine hydrochloride	Cerespan, Pavabid, Pavacap, Pavacen, Vasospan	300 to 600 mg ^b	150	5.50-10.97
Ethaverine hydrochloride	Ethaquin, Ethatab, Laverin	300 to 600 mg ^b	100	7.40-9.90
Niacin (nicotinic acid)	(generic)	250 to 2000 mg ^b	25-500	0.39-4.35
Nicotinyl alcohol	Roniacol	150 to 600 mg ^b	50 150	2.15 6.35
Cyclandelate	Cyclospasmol	400 to 800 mg	100 200	4.20 8.40
<i>Beta Receptor Stimulating Drug</i>				
Nylidrin	Arlidin	9 to 36 mg	6 12	7.08 13.08
<i>Drugs Affecting the Sympathetic Nervous System</i>				
Tolazoline hydrochloride	Priscoline	75 to 200 mg ^b	25 80	4.20 10.60
Moxisylyte hydrochloride ^a (thymoxamine)	Opilon	120 mg	40	—
Phenoxybenzamine hydrochloride	Dibenzyline	20 to 60 mg	10	2.95
Reserpine	Sandril, Serpasil, Rau-Sed, Reserpoid (generic)	0.1 to 1.0 mg	0.1 0.25 0.1 0.25	0.63-2.67 1.05-4.50 0.40-0.81 0.45-1.25
Guanethidine sulfate	Ismelin	10 to 60 mg	10 25	8.40 11.75
Methyldopa	Aldomet	500 to 2000 mg	250 500	6.36 11.45
Dihydrogenated Ergot Alkaloids	Hydergine	4 to 6 sublingual tablets	0.5	9.00

^anot available in the United States^bsustained release drug preparations^cwhen more than one product is available the range of prices is given

receptor stimulating drugs increase muscle blood flow but have little effect on skin flow where only alpha receptors are present. Sympathetic nervous system blocking agents would primarily affect skin vessels since there is little vasoconstrictor tone in skeletal muscle. In evaluating studies of these drugs, several points are important:

1. Was a double-blind, randomized study performed? It must be recognized that patients can often surmise if they are taking an active vasodilator drug because of side effects.
2. Is the drug of benefit during oral administration? Many studies are performed using parenteral, especially intra-arterial, administration. (Placebo injections have rarely been used.) In our studies,³ onset of action of orally administered vasodilator drugs in fasting subjects varied from 15 to 90 minutes, a definite drawback to their use.
3. What happens to systemic blood pressure and pulse rate during exercise after drug administration? There may be dramatic changes with exercise, even when resting blood pressure

and pulse rate are unaffected; few studies have collected these important data.

4. Patients with intermittent claudication do not need an increased muscle blood flow at rest.
5. Objective measurement of an improvement in the circulation is more reliable than patients' subjective responses.

DIRECT-ACTING DRUGS

Isoxsuprine, papaverine, niacin (nicotinic acid), and cyclandelate are representative of a group of vasodilator agents that directly relax vascular smooth muscle. When administered orally these drugs are not potent peripheral vasodilators for any type of vascular disease. Unfortunately, some clinical studies reporting benefit from these agents include patients with a variety of diseases, e.g., venous disease,⁴ leg cramps,⁵ and it is not apparent which underlying diseases were improved; other types of improper design have been noted in many other investigations.

Isoxsuprine. Isoxsuprine was previously thought to increase muscle blood flow by beta receptor stim-

ulation. However, since beta-receptor blocking drugs do not antagonize its vascular effects, isoxsuprine must have a direct action on vascular smooth muscle.⁶ In both animal and normal human studies, isoxsuprine has been shown to increase muscle blood flow; usually skin blood flow has not been affected.^{3,7} It may cause a mild increase in cardiac contractility, heart rate, and cardiac output with palpitations and postural hypotension.⁸ In one placebo-controlled study,⁹ no effect on the systolic pressure gradient in the diseased limb, ankle systolic pressure after exercise, or maximal treadmill walking time was found in 20 patients with obstructive arterial disease taking 20 mg of isoxsuprine or placebo three times a day for four weeks. In a double-blind crossover study,⁷ a single dose of 20 mg did not increase the claudication time on a treadmill or limb blood flow in 12 patients with vascular disease; 7 patients actually had a shorter claudication time after the drug. An uncontrolled study¹⁰ reported improvement in claudication distance in 39 of 46 patients receiving similar oral doses for a median time of seven months; an increase in toe and finger flow was also said to occur with subcutaneous administration of the drug.

In our study,³ oral administration of 40 mg of isoxsuprine to normal subjects in a cool room (20°C) produced a small but significant increase in calf blood flow and no change in foot flow when compared with placebo administration. In 11 patients with femoropopliteal and 5 patients with aortoiliac arteriosclerosis obliterans producing intermittent claudication, no significant changes occurred in calf or foot flow following oral administration of 40 mg of isoxsuprine in a 25.5°C room.¹¹ Measuring muscle blood flow by the disappearance rate of a radioisotope, 2 of 13 patients with femoropopliteal and 1 of 6 patients with aortoiliac disease showed an improvement in their exercise blood flow after isoxsuprine while 2 patients had a definite deterioration in exercise muscle blood flow. In this study, subjective symptomatic improvement during the exercise tests was not apparent. Frequent side effects with the use of isoxsuprine include palpitations, flushing, and postural hypotension.

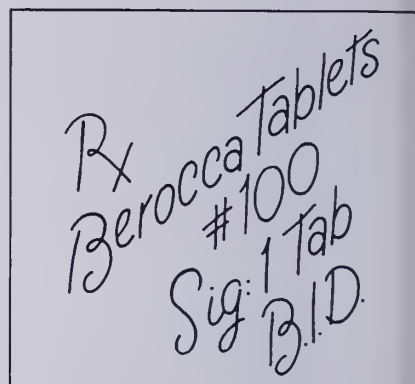
Papaverine. Papaverine and its analogues dilate peripheral arteries in animals and man when administered parenterally, but some investigators have found only small increases in blood flow.^{12,13} Uncontrolled studies of orally administered papaverine have reported either no benefit¹⁴ or good results¹⁵ in patients with intermittent claudication. In patients with Raynaud's phenomenon, an increase in hand blood flow was reported in one study,¹⁶ while another investigation found little change in hand or foot blood flow.¹⁷ Ethaverine has not been extensively studied in peripheral vascular disease but one

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study reported an increase in resting calf blood flow and a decrease in digital blood flow in a group of patients with arterial occlusive disease.¹⁸ Side effects from papaverine and ethaverine include flushing, malaise, gastrointestinal symptoms, and headache. Hepatotoxicity has been reported with papaverine.¹⁹

Niacin and derivatives. Niacin (nicotinic acid) and its derivatives evidently produce more vasodilatation of the blood vessels of the ears, face, and neck than of the extremities.²⁰ In normal man, intravenous niacin may increase hand and forearm blood flow with only a slight increase in leg flow.²¹ Studies have failed to show a consistent increase in skin or muscle flow in patients with obstructive arterial disease.¹⁴ A decrease in skin and muscle blood flow during exercise,²² after exercise, and during reactive hyperemia²³ has been reported. Long-term studies describe either no benefit¹⁴ or symptomatic relief²⁴ in patients with intermittent claudication; one study claimed symptomatic benefit in Raynaud's phenomenon.²⁵ In our study,¹¹ patients with intermittent claudication due to femoropopliteal or aortoiliac arteriosclerotic disease usually did not increase their exercise muscle blood flow after 100 mg of nicotinyl alcohol orally. Side effects from nicotinic acid and its compounds include intense flushing, gastrointestinal symptoms, rash, and postural hypotension.

Cyclandelate. Cyclandelate acts directly on smooth muscles of the blood vessel walls and experimentally has about three times the spasmolytic activity of papaverine.²⁶ Most of the uncontrolled clinical trials report an increased walking distance in about 50 percent of patients with intermittent claudication and less benefit in patients with Raynaud's phenomenon.^{27,28} In a single blind, non-crossover study, patients with femoral artery arteriosclerosis obliterans appeared to improve while patients with iliac disease did not; oscillograph pulse volumes were measured and even this gross test failed to correlate with the subjective responses.²⁹ We did not test cyclandelate in our acute study of vasoconstricted normal subjects because initial experiments showed no increase in foot or calf blood flow with oral doses up to 800 mg. No adequate studies of the clinical effect of this drug are available. If its action is dependent on relief of vasospasm, it is difficult to appreciate how it would benefit patients with obstructive arterial disease. Reported side effects of the drug include headache, flush, gastrointestinal symptoms, drowsiness, and dizziness.

It may be concluded that the direct acting vasodilator drugs have no demonstrated value in the treatment of peripheral vascular diseases.

BETA RECEPTOR STIMULATING DRUG: NYLIDRIN

Nylidrin was modeled after epinephrine and

therefore would be expected to increase muscle blood flow by beta receptor stimulation. Since its action is not entirely blocked by propranolol, it must also have a direct action on the vascular smooth muscle.⁶ In animal and human studies, it increases muscle blood flow when administered parenterally and orally.^{3,30} Most investigators found no significant effect on skin blood flow.^{3,30,31} Variable effects have been reported on heart rate and blood pressure but usually an increased cardiac output and decrease in total vascular resistance have been found.³¹ Uncontrolled studies³² have reported symptomatic benefit in patients with intermittent claudication with oral administration and an increase in postexercise calf blood flow with intravenous drug.³³ Well-controlled studies have found no effect on the clinical symptom of intermittent claudication;^{31,34} variable effects on calf blood flow have been reported.³¹ Both muscle and skin blood flow may be decreased during exercise after intramuscular administration of nylidrin.²² In our study,³ the acute effect of a large oral dose of nylidrin (18 mg) in a cool room in 10 normal subjects was a significant increase in calf blood flow and no change in skin flow when compared to placebo administration. In patients with femoropopliteal arteriosclerotic disease, a significant increase occurred in calf flow at rest; this was not observed in patients with aortoiliac disease.¹¹ Only 1 of 12 patients with femoropopliteal and 1 of 7 patients with aortoiliac disease had an increase in their exercise muscle blood flow after nylidrin ingestion. One of the latter patients had a definite deterioration in exercise muscle flow. Side effects with nylidrin include a sensation of chilliness, flushing, palpitations, nausea and vomiting, and postural hypotension. No evidence is currently available to advocate the use of nylidrin in patients with peripheral vascular diseases.

DRUGS AFFECTING THE SYMPATHETIC NERVOUS SYSTEM

If adrenergically mediated vasoconstriction is important in the pathogenesis of vasospastic diseases or intensifies peripheral ischemia by its normal activity, agents interfering with the action of the sympathetic nervous system could be of value. These drugs include those that block autonomic ganglia and peripheral alpha receptors (tolazoline, phenoxybenzamine, moxislyte), those that interfere with the action of norepinephrine (reserpine, guanethidine, methyl dopa), and those that are either central or peripheral adrenergic blockers (Hydregine, alcohol).

Tolazoline. Tolazoline is an alpha receptor blocking agent which also has a histamine-like effect.³⁵ It has been shown to increase skin blood flow in normal human subjects by parenteral and oral administration.^{3,36} In clinical studies, favorable³⁷ and

unfavorable effects^{14,36} have been reported in disease states; most of these studies are uncontrolled. Of the studies reporting benefit, intra-arterial or oral tolazoline produced relief of rest pain in patients with arteriosclerosis obliterans and healed finger ulcers in patients with Raynaud's disease;³⁷ however, no increase in exercise tolerance occurred. In another study,³⁸ a good response was found in foot blood flow in patients with obstructive arterial disease but only when rest pain was not present. Other studies report very variable results with intra-arterial use and even a decrease in blood flow to ischemic feet in some patients.^{23,36} In our placebo-controlled study,³ 100 mg of tolazoline given orally to normal subjects in a 20°C room produced a significant increase in foot blood flow from an average of 2.3 to 3.1 ml per 100 ml of tissue per minute. When the foot flow of 3.1 ml is compared to the average normal foot flow of 7.3 ml (seen in a warm environment), the action of tolazoline on the vasoconstricted foot is not dramatic. In 10 patients with femoropopliteal and 5 patients with aortoiliac arteriosclerosis obliterans, 75 to 100 mg of oral tolazoline produced no significant change in resting foot or calf blood flow.¹¹ Adverse effects from tolazoline include headache, nausea, chills, flushing, paresthesias of the skin, palpitations, and gastrointestinal disturbances. In our clinical experience, tolazoline has not been of benefit in obstructive arterial disease but is occasionally useful in patients with Raynaud's phenomenon in combination with other agents.

Other alpha receptor blockers, such as phenoxybenzamine and moxisylyte (thymoxamine), have been recommended but are of doubtful benefit.^{36,39} The side effects of phenoxybenzamine (postural hypotension, palpitations, gastrointestinal symptoms) often preclude its use.

Reserpine. Reserpine depletes norepinephrine from the sympathetic nerves; it also possesses a short vasodilatory action, unrelated to norepinephrine depletion, when injected intra-arterially.⁴⁰ In Raynaud's phenomenon, reserpine in doses of 0.25 to 1 mg a day may produce remarkable amelioration of symptoms.^{41,42} In our laboratory, we demonstrated that orally administered reserpine increases capillary blood flow in the fingers in a cool environment in some, but not all, patients with Raynaud's phenomenon or disease.⁴¹ Other investigators have demonstrated that oral reserpine markedly reduced the vasoconstrictor responses in the hand to intra-arterial tyramine and the application of ice to the forehead in patients with Raynaud's phenomenon.⁴² Therefore, the beneficial effect of reserpine is secondary to the attenuation of adrenergic vasoconstriction. Recent reports⁴³ of an increased incidence of breast carcinoma in hypertensive patients on long-term reserpine therapy indicate that the

drug should be used only in the most severe cases until this issue is clarified. Reserpine should never be given to patients with depressive symptoms, or a history of depression. Other frequent side effects besides depression include gastrointestinal symptoms due to increased gastric acid secretion, nightmares, and water retention. Intra-arterial injections of reserpine (0.5 to 1 mg) have been reported to produce more rapid healing of finger ulcers as well as improvement, lasting months, in Raynaud's phenomenon.^{44,45} We have used intra-arterial reserpine only in the most severe cases and have found little improvement over oral therapy. A controlled study⁴⁶ using saline placebo injections did not reveal long-term benefit from intra-arterial reserpine.

Guanethidine. Guanethidine has also been used in patients with Raynaud's phenomenon because it interferes with release of norepinephrine at the sympathetic neuroeffector junction. The original study⁴⁷ used a dose of 30 to 50 mg per day and demonstrated an increased digital capillary blood flow after cooling in patients with Raynaud's phenomenon due to scleroderma. The adverse effect of postural or post-exercise hypotension with this dose prevents its widespread use. With a daily dose of 10 to 20 mg, we have had some success in our patients; other investigators confirm subjective benefit with higher doses.⁴² Other side effects frequently seen with guanethidine are diarrhea, fatigue, and impotence.

Methyldopa. Methyldopa has also been recommended for the treatment of Raynaud's phenomenon. The mechanism of action is probably that methyldopa acts as a false neurotransmitter, replacing the active norepinephrine. Approximately 75 percent of patients ingesting 1 to 2 gm of methyldopa a day reported subjective benefit; this was substantiated by an increased rate of rewarming of digits after cold exposure measured by skin temperatures.⁴⁸ Fluid retention, drowsiness, headache, postural hypotension, nasal stuffiness, and hemolytic anemia may occur with these doses.

Ergot alkaloids. The dihydrogenated alkaloids of ergotamine have an adrenergic blocking effect on the peripheral blood vessels and have been used in patients with peripheral vascular disease. Dihydroergocornine has been shown to increase blood flow to the extremities.^{49,50} Hydergine, an equal mixture of dihydroergocornine, dihydroergocristine, and dihydroergokryptine, induces a significant increase in the blood flow to the hand and foot but small changes in calf blood flow when given intravenously to normal subjects.⁵¹ Ischemic ulcers in patients with obstructive arterial disease reportedly heal somewhat faster during oral Hydergine administration.⁵² However, intermittent claudication was not affected by oral administration of Hydergine⁵² or dihydroergotamine.¹⁴ Intravenous administra-

tion of the latter drug did not benefit 17 patients with intermittent claudication when it was compared to saline injections.¹⁴

Alcohol. Patients with peripheral vascular disease have often been advised that alcoholic beverages may help their circulatory status. Most investigations report a significant vasodilatation in the hand in normal subjects but a variable or decreased blood flow in the calf or forearm.⁵³⁻⁵⁵ In arterial occlusive disease, the effect on blood flow to the toes is variable with poor response in the more severely diseased patients;⁵⁵ indirect evidence indicates alcohol does not affect the collateral vessels.⁵⁶ Although alcohol has been given intra-arterially in the past, there is substantial evidence that it constricts skin and muscle blood vessels by this route of administration.⁵⁴ The cutaneous vasodilatation seen with oral administration of alcohol is apparently mediated via the sympathetic nervous system, for it was absent in sympathectomized or denervated limbs.⁵⁴ Although this action could be central or peripheral, a central action is favored since muscle blood flow is affected in the opposite direction. There is no evidence that alcohol increases blood flow in most patients with obstructive arterial disease; it may help relieve vasospasm.⁵⁶ However, large amounts must often be used and this entails the danger of intoxication. Intra-arterial use of alcohol is contraindicated.

CONCLUSIONS

Review of the clinical studies on vasodilator drugs indicates little substantive evidence that they are effective in the treatment of obstructive arterial disease, either for intermittent claudication or for ischemic rest symptoms and signs. They fail to produce an increase in blood flow in many patients with ischemic limbs, even when administered locally (intra-arterial). Animal studies are in total agreement with clinical studies.^{2,57,58} In normal animals, in which the collateral blood vessels are free of disease, vasodilator drugs may decrease blood flow in the ischemic area induced by obstruction of a main artery.^{57,58} There is also evidence from animal studies that vasodilators can depress the contractile force of skeletal muscle.⁵⁹ In vasospastic diseases, vasodilators that act upon the sympathetic nervous system (i.e., reserpine and guanethidine) may have an ameliorating effect in some patients by increasing cutaneous capillary blood flow. Full benefit from even these agents is prevented by unpleasant and often serious side effects.

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HEALTH CARE DELIVERY IN MAINE II: CONDITIONS EXPLAINING HOSPITAL ADMISSION

Continued from Page 261

depends on physician choice of place and type of treatment. Those choices are made differently among Planning Regions and Hospital Service Areas in Maine with resultant differences in per capita use of hospital beds. Planners who seek to certify the need for hospital facilities should take into account differences in the mix of hospitalized patients. Because questions raised about the need for additional procedures and admissions for specific conditions concern the effectiveness of alternative placements and treatments, answers depend on the status of ambulatory, nursing home as well as hospital resources and these factors need to be taken into account. Since questions about effectiveness are most commonly addressed to members of the medical profession, the review process established to certify the need for facilities should, presumably, involve a panel of physicians to advise on the medical necessity of different levels of use of hospitalized care.

ACKNOWLEDGEMENTS

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Editorial

It has been said that hyaline membrane disease, or idiopathic respiratory distress syndrome, is the most common disorder in premature infants for which high concentrations of oxygen may be prescribed. If the pathophysiologic abnormality of the lungs ameliorates during the administration of oxygen, hyperoxemia may occur and retrolental fibroplasia may develop. Thus, the life of the infant may be saved but the vision sacrificed.

The role of the ophthalmologist in this situation should be two-fold.

First, as a consultant, to be available to examine ophthalmoscopically all premature infants who have received a significant amount of oxygen. The American Academy of Pediatrics has recommended that all infants born at less than 36 weeks' gestation or weighing less than 2,400 gm. (4.2 lb.) who have received oxygen therapy should have their eyes examined at the time of discharge from the nursery and at 3 to 6 months of age.

Second, as a conscience, to remind our colleagues, be they family physicians or pediatricians that the "trade-off" of vision for life is no longer necessary, given our present knowledge of the role of oxygen in the treatment of hyaline membrane disease and the increasing sophistication of the medical and nursing management of this condition. Continuous positive airway pressure, first reported to be beneficial by Gregory et al¹, may so improve oxygenation that significantly lower concentrations of oxygen may be used. Repeated measurement of blood gases, although technically difficult in an ill, premature infant, is essential to monitor the need for high concentrations of inspired oxygen.

These two measures plus careful attention to the nutritional needs and thermal environment of the infant are now usually sufficient to keep the child alive until its lungs develop the ability to produce the pulmonary surfactant which is necessary for normal alveolar function.

The principle of monitoring blood gas concentrations during the administration of oxygen to premature infants with problems other than hyaline membrane disease is equally valid.

One might summarize the interrelationship between infant pulmonary and ocular physiology as follows:

Some problems of neo-natology,
Often involve ophthalmology,
Hyperoxygenation,
Needs close observation,
Before we can sing the Doxology.

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FOR PHYSICIANS' WIVES

THE AUXILIARY TO THE M.M.A. ANNOUNCES THE TRAVELING WORKSHOPS

OCTOBER 20-22 FOR MEMBERS OF ALL COUNTY AUXILIARIES

DISTRICT I – AROOSTOOK, PENOBSCOT, PISCATAQUIS AUXILIARIES

BANGOR — MONDAY, OCTOBER 20
Pilot's Grill, off Interstate 95, Hermon Exit

DISTRICT II – FRANKLIN, KENNEBEC, LINCOLN-SAGadahoc AUXILIARIES

AUGUSTA — TUESDAY, OCTOBER 21
Howard Johnson's, Community Drive off Interstate 95

DISTRICT III – ANDROSCOGGIN, CUMBERLAND, YORK AUXILIARIES

PORTLAND — WEDNESDAY, OCTOBER 22
Northeast Region Red Cross Blood Program Office,
524 Forest Avenue
Brown Bag Lunch — Tour of Facility

REGISTRATION EACH DAY 9:30 a.m.
ADJOURNMENT 1:30 p.m.

Student Nurses and Smoking

A Survey

MARSHALL F. BURK, B.S.* and GEORGE T. NILSON, S.M., M.P.H.**

Each year more than 300,000 Americans die prematurely from the effects of smoking. Millions more live on with crippled lungs and overstrained hearts. Cigarette smoking is a major cause of emphysema, chronic bronchitis, lung cancer and heart disease.

There is no controversy about these facts. They have been documented by hundreds of careful studies.^{1,2}

Almost a million teenagers take up smoking every year. More women are smoking than ever before and studies show that they find it harder to quit than men do. Smoking, like other learned behavior, is difficult to modify.

A 1974 survey "Smoking Habits of Maine Health Professionals" indicates that younger physicians (M.D.'s) are smoking less than older physicians. According to the Maine Department of Health and Welfare Survey,³ the percentage of M.D.'s under 50 years of age that are smokers is only 14.1%, while 22.6% of the doctors over 50 are still smoking. The average of the total group of M.D. respondents was 18.7% smokers.

Among nurses who participated in the survey, this relationship was found to be reversed. Nurses under 50 years of age showed 30.2% smokers. Nurses over 50 years only 22.7%. The average of the group was 27.6% smokers.

The largest group of health care providers is the nursing profession. The question occurred to us, "how could we, as a voluntary health agency deeply concerned with the terrible toll of "cigarette disease" upon our society, enlist more nurses to become aware of the important role that they have as exemplars and as health educators vis-a-vis smoking?"

As a means of securing involvement and to obtain baseline information, it was decided to conduct a survey of the entering first year students among the Nursing and Licensed Practical Nursing Schools of Maine. A total of nine nursing schools cooperated in the study and 421 first year students completed questionnaires in the fall of 1974. The questionnaire was designed to obtain the following information: (1) Percentage of student nurses who currently smoke, ages that they began smoking and their level of cigarette consumption; (2) identify the respon-

dent's reasons for starting smoking; (3) determine student-nurse attitudes toward: smoking, sale of cigarettes in medical facilities, exemplar role of the nurse and the rights of nonsmokers; (4) assess student nurses' knowledge of the relationships of smoking as a causal factor in the development of certain diseases.

The survey findings are summarized as follows:

The Percentage of Students Who Currently Smoke

	<i>No. of Students %</i>	
1. Kennebec Valley School of Practical Nursing	41	39.0
2. St. Joseph's College, North Windham	40	65.0
3. Mercy Hospital, Portland	42	31.0
4. Westbrook College	48	50.0
5. Central Maine Vocational Institute, Auburn	40	30.0
6. St. Mary's General Hospital	46	23.9
7. Eastern Maine Medical Center	43	41.9
8. Central Maine General Hospital	68	30.9
9. University of Maine, Augusta, Division of Nursing and Health Sciences	53	32.1
Total	421	37.5

The percentage of student smokers in the above nine schools ranges from a low of 23.9 percent to a high of 65.0, with an average of 37.5 percent. This average approximates the findings of a national random sample survey of professional nurses conducted in 1969 by the National Clearing House for Smoking and Health which found that 37.3 percent of the nurses were smokers.

Ages That Students Began Smoking

Less than 12 years	3.5 percent
12-14	24.1
15-17	50.6
18-20	13.5
21 plus	2.9
No answers	5.3

As the above figures show, the majority of smokers began to smoke between the ages of 15 and 17 years old. Interestingly, 3.5 percent stated they started before the age of twelve, some as early as eight years old.

*Program Director, Maine Lung Association, (formerly Maine Tuberculosis and Health Association)

**Executive Director, Maine Lung Association

<i>Level of Cigarette Consumption Per Day</i>	
1-10 cigarettes	31.8 percent
11-20	45.2
21-30	17.2
31-40	5.8
40 plus	none

The level of cigarette consumption on a per day basis showed that none of the respondents smoked more than two packs. A majority of 77 percent smoked one pack or less per day.

<i>Reasons for Starting to Smoke</i>	
Peer pressure	44.9 percent
Maturity	8.2
Don't know	4.4
Like taste	5.7
Lose weight	1.9
Other	24.1
No answer	10.8

The reasons given for starting to smoke were varied, including nervousness, desire to look older, to lose weight, do something with hands. The reason most often stated, however, was 'keeping up with the crowd.'

<i>Percentage of Responding Smokers Who Have Tried to Stop</i>		
YES	78.3 percent	Number of Times:
NO	21.7	1 23.0
		2-4 48.7
		5 plus 13.5
		No answer 14.9

Three out of four admitted smokers, or 78.3 percent, claimed that they had tried to quit the habit. Interesting, too, is the 13.5 percent who stated they had tried five or more times. The most frequent reason given for quitting or reducing cigarette consumption was the concern for health. This concern was expressed by 47.9 percent of the respondents. 7.3 percent quit or cut down on smoking due to family pressure, while 19.4 percent were motivated by the cost of the cigarette habit.

<i>Now a Nonsmoker or Cut Down - Why?</i>	
Concern for health	47.9 percent
Family pressure	7.3
Expense	19.4
Other	25.5

<i>Do you think nurses have a role in educating patients about the effects of smoking?</i>	
YES	94.3 percent of smokers — 97.3 percent of nonsmokers

Are you interested in learning to help the patient
Continued on Page 273

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or Narcan® (naloxone HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonsfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

SEARLE

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San Juan, Puerto Rico 00936

Address medical inquiries to:
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When diarrhea
has him reeling...



Diarrhea can hook anyone. When it does, physicians and patients both want prompt control of diarrheal symptoms. Lomotil will usually control diarrhea promptly.

This rapid action can halt the emergency aspect of diarrhea and is comforting and reassuring to the patient. Electrolyte and

fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate specific therapy should be given along with Lomotil.

Lomotil is contraindicated in children less than 2 years old.

Lomotil[®] TABLETS LIQUID

Each tablet and each 5 ml. of liquid contain: diphenoxylate hydrochloride 2.5 mg (Warning: May be habit forming), atropine sulfate 0.025 mg

holds the line.

In hypertension,

ALDOMET[®] (METHYLDOPA|MSD)

usually offers more
than effective lowering
of blood pressure...

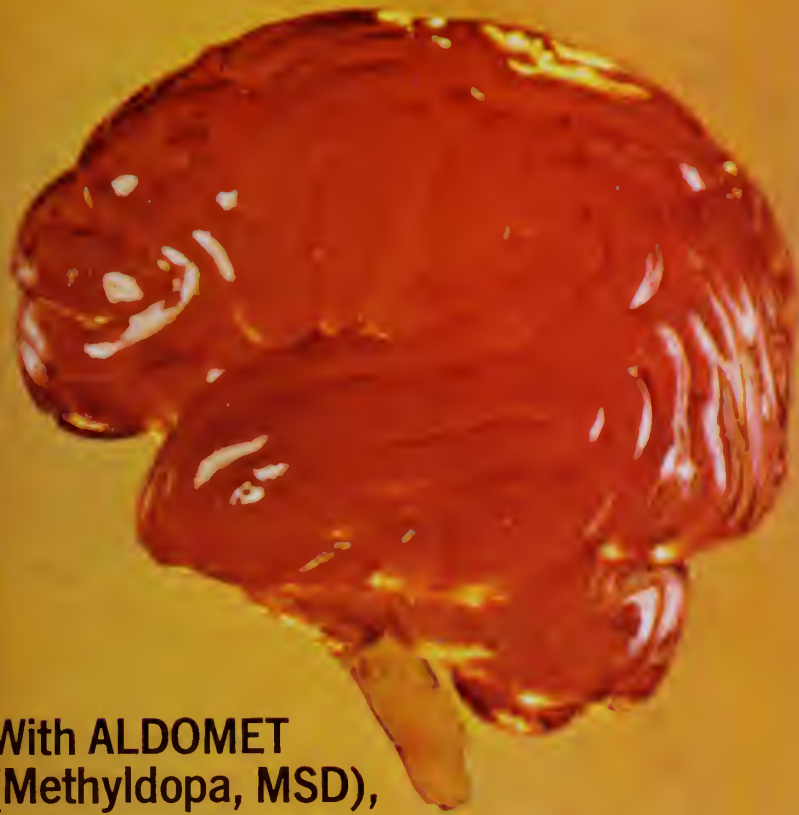


**With ALDOMET
(Methyldopa, MSD),
existing renal function
is usually unchanged**

ALDOMET has no direct effect on renal function. When used in effective doses, ALDOMET usually does not reduce glomerular filtration rate, renal blood flow, or filtration fraction.

**With ALDOMET
(Methyldopa, MSD),
cardiac output is
generally unchanged**

ALDOMET has no direct effect on cardiac function. When ALDOMET is used in effective doses cardiac output is usually maintained with no cardiac acceleration; in some patients the heart rate is slowed.



With ALDOMET (Methyldopa, MSD), symptomatic postural hypotension is infrequent

ALDOMET reduces both supine and standing blood pressure. Less frequent symptomatic postural hypotension is experienced with ALDOMET than with many other antihypertensive agents. Exercise hypotension and diurnal blood pressure variations rarely occur.

for hypertension

TABLETS, 250 mg, 500 mg, and 125 mg

ALDOMET[®] (METHYLDOPA|MSD)

a unique antihypertensive agent

ALDOMET is contraindicated in active hepatic disease, hypersensitivity to the drug, and if previous methyldopa therapy has been associated with liver disorders. It is not recommended in pheochromocytoma. It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

For a brief summary of prescribing information, please see following page.

to further
simplify therapy
for many patients

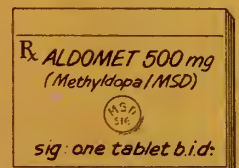
now available
ALDOMET[®] 500 mg
(METHYLDOPA|MSD)

- often more practical to prescribe
- easier for patients to remember

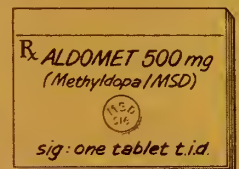
Now offered in addition to the standard 250-mg tablet, the new ALDOMET 500 mg tablet is a patient convenience. An especially important one, since in hypertension convenience of the dosage schedule is one factor that can make the difference in compliance of the patient. The minimum daily dose of ALDOMET is 250 mg b.i.d. The usual starting dose is 250 mg t.i.d. Dosage is adjusted as necessary by adding or deleting 250 mg or 500 mg at intervals of not less than two days. The maximum dose is 3.0 g per day.

Examples of b.i.d. or t.i.d. dosage convenience provided by ALDOMET 500 mg within the usual daily dosage range of 500 mg to 2.0 g:

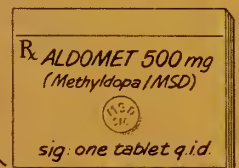
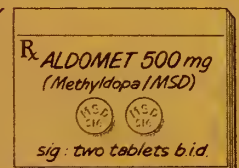
1.0-g
daily
dose =



1.5-g
daily
dose =



2.0-g
daily
dose =



NOTE: Tablets shown are not actual size.

in hypertension

ALDOMET[®] (METHYLDOPA|MSD)

usually lowers blood pressure effectively



Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyl dopa therapy has been associated with liver disorders (see Warnings); hypersensitivity.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyl dopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyl dopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyl dopa. If a positive Coombs test develops during methyl dopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyl dopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyl dopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyl dopa, the drug should not be reinstituted. When methyl dopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyl dopa is stopped.

Should the need for transfusion arise in a patient receiving methyl dopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or

cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyl dopa. If caused by methyl dopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyl dopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reaction or unusual manifestations of drug idiosyncrasy.

Use in Pregnancy: Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyl dopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyl dopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyl dopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyl dopa because the drug is removed by this procedure.

Adverse Reactions: *Central nervous system:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, involuntary choreoathetotic movements; psychic disturbances including nightmares and reversible mild psychoses or depression.

Cardiovascular: Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyl dopa if edema progresses or signs of heart failure appear.)

Gastrointestinal: Nausea, vomiting, distention, constipation, flatus, diarrhea, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis.

Hepatic: Abnormal liver function tests, jaundice, liver disorders.

Hematologic: Positive Coombs test, hemolytic anemia, leukopenia, granulocytopenia, thrombocytopenia.

Allergic: Drug-related fever, skin rash.

Other: Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, mild arthralgia, myalgia.

Note: Initial adult dosage should be limited to 500 mg daily when given with antihypertensive other than thiazides. Tolerance may occur, usually between second and third month of therapy; increased dosage or adding a thiazide frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

How Supplied: Tablets, containing 125 mg methyl dopa each, in bottles of 100; Tablets, containing 250 mg methyl dopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyl dopa each, in single-unit packages of 100 and bottles of 100.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck Co., Inc., West Point, Pa. 19486

MSD MERCK SHARP & DOHME

with a smoking problem?

YES 95.6 percent of smokers — 98.1 percent of nonsmokers

The questions concerning the 'exemplar role' of the nurse, received positive answers from both smokers and nonsmokers alike.

Do you think nurses should discourage patients from smoking?

YES 71.5 percent of smokers — 86.9 percent of nonsmokers

NO 25.3 percent of smokers — 11.9 percent of nonsmokers

In your opinion — Why is it that a large percentage of nurses smoke?

Pressure of work 22.3 percent

Inability to break the habit 54.5

Disbelief of causal relationship between smoking and ill health 7.8

Other 15.1

No answer 1.2

'Inability to break the habit' accounts for 54.5 percent of the opinions why nurses smoke.

Should hospitals and other public medical facilities allow smoking?

Only in specially designated areas — 84.8 percent of smokers — 78.9 percent of nonsmokers

YES, No restrictions on smoking — 6.3 percent of smokers — 2.3 percent of nonsmokers

NO smoking allowed — 8.9 percent of smokers — 18.7 percent of nonsmokers

While very few would place *no* restrictions on smoking in hospitals and other public medical facilities, the majority would allow smoking only in specially designated areas.

Should hospitals and other public medical facilities allow the sale of cigarettes within the facility?

YES 36.9 percent of smokers — 15.2 percent of nonsmokers

NO 20.3 percent of smokers — 38.7 percent of nonsmokers

Only in coffee shops: 42.7 percent of smokers — 46.1 percent of nonsmokers

Almost twice as many nonsmokers as smokers were against the sale of cigarettes. A majority of both smokers and nonsmokers favored the sale of cigarettes only in the coffee shops.

Are you bothered by tobacco smoke?

YES 9.5 percent of smokers — 63.2 percent of nonsmokers

NO 45.6 percent of smokers — 8.1 percent of nonsmokers

Sometimes: 44.9 percent of smokers — 28.7 percent of nonsmokers

Do health professionals: doctors, nurses, therapists, etc. have a responsibility to set a good

example by not smoking in public?

YES 45.0 percent of smokers — 66.0 percent of nonsmokers

NO 23.9 percent of smokers — 10.2 percent of nonsmokers

No opinion: 31.1 percent of smokers — 23.8 percent of nonsmokers

Recognition of relationship of smoking to certain diseases

Major cause

Lung cancer 74.9 percent

Pulmonary emphysema 52.4

Chronic bronchitis 52.4

Laryngeal cancer 48.9

Oral cancer 45.1

Contributing Cause

Coronary Artery Disease 48.6 percent

Any soft tissue lesion 39.2

Leukoplakia 34.5

Can't Say

Neo-natal death 50.6 percent

Bladder cancer 47.1

Peripheral vascular disease 42.3

SUMMARY AND COMMENTS

The level of smoking among the Maine student nurses surveyed in 1974 approximates that of a national random sample of professional nurses surveyed in 1969,⁴ i.e., 37.3 percent.

The survey reinforces, we think, the need to incorporate a specific learning experience regarding cigarette smoking and health in the nursing curriculum rather than assume that the subject will be adequately covered within the regular nursing curriculum. A resurvey of as many of the same student nurses as possible at the time of graduation is planned in an attempt to assess the impact of the nurse education program on smoking attitudes and habits. Analysis of significant changes that are found may provide useful clues for improving the educational program against smoking.

Despite the relatively high percentage of student nurses who smoke, it is encouraging to note their apparent acceptance of the notion that nurses have a role in educating patients about the effects of smoking and that they are interested in learning how to help the patient with a smoking problem.

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Hemothorax Complicating Anticoagulation for Pulmonary Embolus

A Report of 2 Patients

FRANKLIN E. BRAGG, M.D.*

SYNOPSIS-ABSTRACT

Hemothorax was a complication of anticoagulation therapy for acute pulmonary embolus in two patients. Anticoagulation was not excessive in either. This unusual complication is described to heighten awareness of its occurrence.

Hemorrhagic complications of anticoagulant therapy are regrettably common. Surprisingly, hemothorax, complicating anticoagulation for pulmonary embolization, has been reported infrequently.¹⁻⁶ The following are case reports of 2 patients in whom a massive hemothorax developed while being anticoagulated for pulmonary embolus.

CASE REPORTS

Case 1. A 56-year-old woman was admitted on November 21, 1973, with a 36-hour history of left anterolateral pleuritic chest pain without associated cough, hemoptysis or shortness of breath. In 1968, she developed a Coombs positive hemolytic anemia with one of twelve L-E cell preparations positive; antinuclear antibody titer at 1:8; RA test negative; and skin, muscle and lymph node biopsy normal. Sixty milligrams a day of Prednisone reduced the hemolysis but induced diabetes mellitus which was treated with oral agents. Because of persistence of a high reticulocyte count, splenectomy was carried out and since that time she had remained well, off all medications except Menest® 1.25mg daily for post pan-hysterectomy menopausal symptoms.

Two weeks prior to her current admission, the patient fractured her left tibia and fibula requiring a long leg cast and bed rest. On admission she was afebrile, in moderate distress with chest pain and tachypnea. Physical exam revealed dry, crackly râles at both bases posteriorly without a friction rub, the murmur of aortic stenosis without a gallop or accentuation of the pulmonic component of the second heart sound, and no evidence of phlebitis in the right leg or left groin. Laboratory studies showed: Hematocrit, 38%; platelets, adequate on smear; reticulocytes, 2.1%; white blood cell count (WBC), 13,700/cu mm without a shift to the left; urinalysis, electrolytes and electrocardiogram (ECG) normal; sedimentation rate uncorrected, 47; direct Coombs test, 4+ positive; rheumatoid arthritis test and serology for syphilis, negative; antinuclear antibodies, 1:4; blood urea nitrogen (BUN), 9; bilirubin (total), less than 1.0; fasting blood sugar, 115; partial thromboplastin time 21 sec (control 26 sec); and stool for occult blood, negative. Chest x-ray on admission showed haziness at the left costophrenic angle and a companion lung scan showed a perfusion deficit in the left upper anterior lung field. Arterial blood gases on room air were pH 7.41, pO₂ 55mm Hg, pCO₂ 45mm Hg.

Intravenous heparin (sodium) and oral (sodium) warfarin

*From the Medical Service, Eastern Maine Medical Center, Bangor, Maine 04401.

TABLE 1

ANTICOAGULANT DOSAGE AND COAGULATION PARAMETERS FOR CASE 1				
Date	Heparin Units IV Every 4 hours	(Tube 3, Minutes) Lee-White Clotting Time	Coumadin® (mg p/day)	Prothrom- bin Time (%)
Nov. 21	5000	11	10	90
Nov. 22	5000	20	10	90
Nov. 23	5000	23	10	49
Nov. 24	5000		10	43
Nov. 25	5000		5	32
Nov. 26	5000	19	7.5	40
Nov. 27	5000		5	32
Nov. 28	5000	19	2.5	27
Nov. 29	5000		2.5	29
Nov. 30	5000		0	26
Dec. 1	D/C	39	0	19
Dec. 2		38	0	25

therapy were started. The doses and clotting parameters are recorded in Table 1.

The partial thromboplastin time was not repeated. No other drugs except meperidine were administered.

On November 26, a repeat chest x-ray showed a definite infiltrate at the left base posteriorly. That evening the patient developed worsening of her pleuritic chest pain which had been improving. Physical exam revealed dullness at the left base posteriorly while ECG showed sinus tachycardia. By November 28, she was febrile. On November 29, chest x-ray and physical exam revealed a large fluid collection in the left thorax. Thoracentesis on November 30 produced only a few cubic centimeters (cc) of blood while on December 2 repeat thoracentesis yielded 550cc bloody fluid with a hematocrit of 16% (blood hematocrit, 26%) and a negative culture. Heparin was discontinued. A chest tube was placed in the left chest December 3 with drainage of another 200cc bloody fluid but chest x-ray showed almost complete opacification of the left lung field. The chest tube was removed on December 15, having drained only small amounts of serosanguineous fluid.

Warfarin was restarted on December 4 and continued without complication for seven months on an outpatient basis. A chest x-ray taken July 2, 1974, showed only minimal fibrotic streaking at the left base.

Case 2. A 30-year-old white woman was admitted January 2, 1974, for acute appendicitis requiring appendectomy. Surgery was uncomplicated and recovery uneventful. At home on January 11, she suddenly developed right chest pain while watching television and was readmitted with cough and hemoptysis. She was afebrile, in mild distress with pleuritic chest pain and a cough but had no abnormal findings on complete examination. Pelvic examination by a gynecologist revealed only a green frothy vaginal discharge consistent with trichomonas vaginitis.

TABLE 2
ANTICOAGULANT DOSAGE AND COAGULATION
PARAMETERS FOR CASE 2

Date	Heparin Units IV Every 4 hours	(Tube 3, Minutes) Lee-White Clotting Time	Coumadin* (mg po/day)	Prothrom- bin Time (%)
Jan. 11	7500			81
Jan. 12	7500	21		
Jan. 13	8500	9	10	81
Jan. 14	8000	42	10	43
Jan. 15	8000	32	5	40
Jan. 16	8000	19		34
Jan. 17	D/C			74

Chest x-ray showed an elevated right diaphragm with atelectasis at the right base. Electrocardiogram was normal. Arterial blood gases on room air were: pH 7.46, pO₂ 70mm Hg, pCO₂ 34mm Hg. Additional lab data included: Hematocrit, 41%; WBC, 15,200 with a normal differential; platelets, adequate on smear; urinalysis showed pyuria; urine culture, many diptheriods and a rare gram negative rod; electrolytes, normal; BUN, 12; and fasting blood sugar, 85. On January 12, lactic acid dehydrogenase was 111 units (normal 29-92).

She was started on intravenous heparin and oral warfarin as shown in Table 2. The only other drugs given were meperidine for chest pain and metronidazole 250mg 3 times a day starting on January 15 for trichomonas vaginitis.

By the third hospital day, she was more comfortable but febrile. On January 15, an increase in the chest pain occurred, her hematocrit dropped from 37% in the morning to 33% by evening and chest x-ray showed a large accumulation of fluid in the right thorax. The next day the fluid in the right thorax had increased by physical exam and x-ray. Repeated thoracenteses yielded only 5cc's of bloody fluid which was culture negative. Both heparin and warfarin were discontinued and 20mg phytonadione (Aqua-Mephyton®) was given intravenously. She improved steadily and was discharged fully ambulatory January 21.

Five days later she was readmitted with increased cough, right chest pain and shortness of breath. She was afebrile but did have a pleural friction rub in the right lateral chest. Chest x-ray showed the same large amount of fluid in the right thorax, lung scan showed a perfusion deficit only at the right base, and the hematocrit was 34%. Ambulation was continued, analgesics were administered and one week later she was sent home again with an uneventful recovery. Chest x-ray on June 27, 1974 showed fibrotic streaking and a small rounded density at the right lung base which was thought to represent a slowly resolving fluid collection.

DISCUSSION

Case 1 was predisposed to thrombophlebitis by the immobilization imposed by a long leg cast. Although fat embolization has not excluded, and spontaneous hemothorax has been reported to occur in systemic lupus erythematosus without anticoagulation,⁷ it is assumed that thrombophlebitis in the left leg with clot embolization occurred

even though no obvious site of thrombophlebitis was discovered (the left leg could not be examined). Retrospectively the hemothorax is thought to have started to accumulate on November 26, a day when her anticoagulation was not excessive.

Case 2 was predisposed to thrombophlebitis by abdominal surgery for acute appendicitis. Once again no obvious site of thrombophlebitis was found, but clot embolization is presumed to have occurred. Her hemothorax developed on January 15 when her anticoagulation parameters were within the "therapeutic range" or slightly high.

The therapeutic dilemma presented by both these patients was whether to continue anticoagulation to prevent subsequent potentially fatal pulmonary emboli or to stop the anticoagulation to avoid progression of a potentially fatal hemothorax. Case 1 was placed back on oral anticoagulants after a 4-day hiatus because it was felt that the immobility imposed by a long leg cast would continue to predispose her to thrombophlebitis and fatal pulmonary emboli.

Case 2 was not anticoagulated again because her predisposition to thrombophlebitis was thought to be reduced with the surgery already 2 weeks away and the patient fully ambulatory.

Although both these patients may have had an abnormally elevated partial thromboplastin time (evidencing excessive suppression of Factor IX by the warfarin), it appears that they developed a hemothorax without excessive anticoagulation. With good laboratory control of anticoagulation, hopefully this complication can be kept at an irreducible minimum and with heightened awareness of its possible occurrence, earlier clinical recognition may help to keep its mortality as low as possible.

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Interactive Television and the Rural Family Physician

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DEAN J. SEIBERT, M.D., HAROLD F. PYKE, M.F.A. and WARREN KYPRIE, B.S.

In the search for answers to the shortages and maldistribution of health care services and personnel, several solutions have been proffered: more medical schools training more physicians; new para-professionals such as physician's assistants or MEDEX¹ and nurse practitioners;² and various exotic technologies, including computerized algorithms,³ lasers, satellites,⁴ and closed circuit television.⁵ At this point in time, television, having been subjected to diverse field trials over the past decade, has proven to be both acceptable and efficient.

Health care shortages are experienced in microcosm within the states of New Hampshire and Vermont and are further exacerbated by the characteristics of rural life, such as rugged terrain with few good roads, severe winter conditions, and far flung population centers. In the effort to overcome these obstacles to quality health care, interactive television has been utilized as a demonstration model to provide medical education, service, and consultation to family physicians and other health care workers in New Hampshire and Vermont.

Funded by the Lister Hill National Center for Biomedical Communications (National Library of Medicine), Interact, the Interactive Television Network of Dartmouth Medical School, provides a microwave, closed circuit television system currently linking two medical centers, three community hospitals, a state prison, and a vocational-technical college. Each of these facilities participating in the network share their resources with each other — resulting in a large pool of information and service that is almost immediately available.

Interact has three major goals — medical education, certain direct medical services, and consultation. In the accomplishment of these goals, each facility has wired rooms for closed circuit television, remote and mobile cameras, monitors, videotape recorders, x-ray view boxes, slide screens, writing easels and other ancillary equipment. Thus, each facility serves as a resource center for each other.

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MEDICAL EDUCATION

The demand for continuing medical education (CME) for health professionals is becoming more widespread. The State of Washington now requires a specified amount of CME involvement for relicensing physicians. The medical societies of New Mexico and Pennsylvania are considering legislative action to provide CME for physicians. The Board of Commissioners of the Joint Commission on Accreditation of Hospitals now requires that the medical staff provide a continuing program of professional education, or give evidence of participation in such a program. Taking a different approach, the AMA has sponsored a voluntary CME incentive program: the American Medical Association Physician's Recognition Award. During the first three years of this program, approximately thirty thousand physicians qualified for the award.

Typically, the family physician in a rural area experiences some inconvenience, if not great difficulty, in keeping abreast of recent developments in medicine, in finding time to read medical journals, in scheduling convention meetings into his already overburdened work schedule. In many areas, distance makes travel impractical and winter conditions frequently make it arduous if not impossible.

The Network has attempted to offer family physicians in the rural community greater accessibility to CME by establishing television links in community hospitals remote from medical schools. Consequently, the physician who is geographically isolated from a medical center and its educational opportunities can have ready access to it via his nearest hospital in the link.

The Network provides daily educational programs approved for elective credits by the American Academy of Family Practice. Efforts are currently being directed toward offering prescribed credits as well.

Allied health workers, such as Nurses,⁶ Physical and Inhalation Therapists,⁷ Social Workers, Ambulance drivers and other paramedical personnel have been included in the educational effort by additional programs designed to meet their particular needs.

MEDICAL SERVICE

In terms of providing medical service to outlying geographical areas, it becomes readily apparent that



Fig. 1 shows an informal educational seminar between physicians at Claremont, N.H. and Hanover, N.H.

when the patient population is scattered about in communities either too small to fully utilize a resident physician, or too widely separated to be easily visited, then the inherent advantages of telemedicine may themselves justify the greater expense.

In fact, the initial endeavor of the network was to provide psychiatric consultation and service from Dartmouth Medical School to Claremont, N.H. — the largest town in Sullivan County. Neither the town nor the county had a resident psychiatrist. The evidence from this early project seemed to justify the conclusion that interactive television provides a means of psychiatric interviewing at a distance with a diagnostic and therapeutic effectiveness approximating that which is obtainable in in-person interviewing.⁸ Since 1968, psychiatric services have been one of Interact's most important medical services.

It might seem that the defined characteristics of interactive television would restrict its use in the provision of direct medical services to those modalities in which sight and sound are the prime determinants of diagnosis and treatment, such as psychiatry. Fortunately, this is not true. With the addition of ancillary personnel, for example, a MEDEX, Interact has been able to provide dermatological services to a community without a dermatologist. A trained paraprofessional is needed at the patient's end of the television link to perform such activities as patch testing, acne surgery, lesion palpation, and so on. The MEDEX acts as the hands of the dermatologist, who can only see and hear the patient. A year and a half's experience in providing televised dermatological services has indicated that it can be both effective and efficient.⁹

Similarly, in the provision of speech therapy services by television,¹⁰ it becomes necessary to have paraprofessionals at the patient's end of the link.



Fig. 2 shows a dermatologist conducting an interview with the patient and the MEDEX.

Certain procedures require a "hands on" experience where someone, speech pathologist or speech aide, needs to physically touch the patient. For example, touching the tongue-teeth with a tongue blade, pinching the nares, tilting the head and spreading the lips to allow the camera to zoom in for examination of teeth, tongue, tonsils and so on — all are facilitated by direct physical manipulation. Such activities can easily be taught speech aides, who can perform these activities at the remote location with the speech pathologist observing.

Thus, the advantages of a paraprofessional in a rural area backed up by specialists via television are many and they offer a partial solution to the lack and maldistribution of medical professionals. With such paraprofessionals, Interact expects to expand its medical services beyond psychiatry, dermatology, and speech therapy.

CONSULTATION

Family physicians in the community and specialists in the medical centers have held consultations over the Interact network in such areas as psychiatry, pediatrics, neurology, radiology, gastroenterology, oncology, and surgery. During these consultations, x-rays and slides can be shown over the television or an electronic stethoscope may transmit heart sounds. Frequently they take the form of the traditional case presentation.

A recent innovation in consultation has been an informal breakfast hour between family physicians in Claremont, N.H. and the Chairman of the Department of Medicine at Dartmouth Medical School. The community physicians telephone the Chairman's office during the week to specify what problems or difficult cases they would like to discuss. The Chairman then invites appropriate specialists from the medical center to join him during the Friday morning breakfast hour to add



Fig. 3 shows a tumor consultation between a physician at Dartmouth-Hitchcock Medical Center and physicians at Claremont General Hospital.

their expertise to the particular topic under consideration. This joint planning and mutual involvement has been particularly effective in making this program a successful prototype for similar programs in the future.

This joint involvement in the planning of future interactions — whether they are educational or consultative, formal or informal — has proven to be a crucial concept in interpersonal relationships. All too frequently the tender egos of family physician and medical school specialist become bruised by real or imagined slights, by misperceptions left unchallenged, and by bids for status and prestige.¹⁰ Joint involvement nurtures equality and tends to diminish misperceptions. Also, a sense of ownership is generated, which tends to increase incentive and motivation. Of further importance is the fact that plans made jointly tend to be more relevant and suited to the needs of the participants than when they are left to one person's assumptions or second guessing process.

When a family physician in the community has a patient for whom he feels a psychiatric consultation is needed, he can arrange for the consultation to take place over television. Following the physician's telephone call to the medical center requesting the consult, the psychiatrist and the family physician with the patient go to the T.V. studios in their respective hospitals. A remotely controlled camera and monitors at both locations allow each to hear and see the other in private; no cameramen are necessary and the closed circuit mode prevents other stations from listening in. After introductions and a brief history, the family physician may go into an adjoining room where he can observe the interchange between the psychiatrist and patient over a split screen monitor. At the end of the consultation, the physician may return to the studio and talk with the psychiatrist regarding medication, management,

or referral while the patient goes to the waiting area. This televised consultation process permits the physician to become directly and immediately involved in the process, to have immediate feedback, to establish rapport, and to retain control over his patient — elements which are difficult to obtain by telephone or mail.

Face-to-face tumor consultations between family physicians in the community and oncologists at the medical center are televised regularly. During the consultations, the patients themselves may be presented as well as their x-rays shown. Again, feedback to the family physician is immediate. Frequently this procedure saves the patient an unnecessary trip to the medical center.

An additional benefit to televised consultation is the appropriateness of referral. The family physician soon discovers exactly what kinds of referrals the various departments of the medical center want, what they are equipped to deal with, and what procedures they typically utilize. An inappropriate referral is wasteful for everyone, but all too often communication barriers are such that they engender ambiguity or misinformation. The capability of interaction over television from distant communities allows physicians to receive and offer immediate and accurate perceptions.

AVAILABILITY AND ACCESSIBILITY

One of the important lessons that Interact has learned regarding utilization of the network revolves around the concepts of availability and accessibility. Merely because educational programs and services are available somewhere, the busy physician may not take advantage of them. The key to utilization is accessibility, the immediacy of obtaining that which is desired. For example, the Dartmouth-Hitchcock Medical Center has long held educational meetings and symposia, which physicians throughout the state could attend if they wished. However, attendance by non-Dartmouth physicians has been sporadic. Now, with many of these meetings televised throughout the network, the community physician has only to go to the nearest participating facility to take part in a program. Attendance has recently soared.

Accessibility operates with patients in a similar manner. One hundred and ten consecutive patients to the televised dermatology clinic were asked what they would have done if the TV clinic was not available. Thirty-three percent replied that they did not know, they would have done nothing, or they would have treated themselves. These thirty-three percent came for treatment because it was easily accessible. Again, accessibility means use.

CONCLUSION

The experiences of Interact indicate that closed

circuit television is one solution to the shortages and maldistribution of health care personnel and services. In the face of long distances, uncooperative terrain and weather, interactive television can bring quality medical education, medical services, and consultations on an as needed basis to those medical communities that lack them.

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Emergency Division Physician

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The First Six Months After Otitis Media

A Preliminary Report

COLLEEN TAYLOR, R.N., P.N.A.* and DANIEL K. ONION, M.D., M.P.H.*

SUMMARY

Eighty-nine children with otitis media were observed for six months. Transient hearing impairment occurred in 24%. Ninety-eight percent had cleared clinically by three weeks. More than one-third had a second attack and more than one-third of these patients had a third recurrence within the six months. The male/female ratio was nearly equal for first attacks but males had more recurrences. Those patients who did not take all of their medicine in a prescribed manner had fewer recurrences.

INTRODUCTION

Otitis media is a very common diagnosis in a primary care practice. The disease is relatively precisely defined by historical and physical examination data, and its treatment is effective.¹ If not treated, it probably leads to significant hearing loss in many children. Even when treated appropriately, temporary hearing deficits occur in more than one-half, and permanent loss may result in 10% of the patients or more.² Acute hearing capability is crucial to a child's success in school.³ The use of antibiotics has markedly diminished other serious complications of otitis media like mastoiditis, facial nerve damage and meningitis. But the disease is still a serious one. Hearing loss complications can be easily overlooked in a busy practice which focuses on acute illnesses.

We codified our general approach to otitis media two years ago in the form of a rough protocol. The protocol defines the essential diagnostic criteria and prescribes a treatment and follow-up regimen. Using this protocol, we began documenting our experience with otitis media in our practice in order to compare it with the published experiences in other practices.

METHODS

All local cases of otitis media seen by one of us (CT) were tabulated. To make the diagnosis, we required an inflamed, dull tympanic membrane with poor pneumatic movement in a compatible clinical setting. Cases with a perforated drum were not included.

All cases were treated with oral antibiotics for ten days. Children under one year of age were treated with ampicillin alone, those one to three years old,

with ampicillin and a decongestant, those over three years with penicillin and a decongestant. If a history of penicillin allergy was elicited, erythromycin was substituted and sulfisoxazole also added if the child was under three.

All cases were re-examined at two weeks. If the inflammation and/or dullness had not resolved, or if the drum's pneumatic movement was poor, then the patient was asked to return in another week. At that point (21 days after initial diagnosis), if the ear was still abnormal, the patient was referred to an ear-nose-throat physician. Screening audiograms were performed in children over four, between two and three weeks after initial diagnosis. If abnormal, these were repeated at three months. The audiograms were performed by a public health nurse using an Audi 1969 Maico Audiometer® with a sensitivity of 30 decibels at 250-8000 cps. Twenty-one of 23 children over four had audiograms.

Patients were asked to bring prescription bottles with them to the two week follow-up appointment. Compliance in taking the prescribed medicines was estimated from the unused amount. If more than 10% of patients' medicines remained, they were judged relatively non-compliant.

After tabulating data for a year, we have examined the first six months experience of each of our first 89 cases. Most patients returned to the same provider (CT) when recurrent illness occurred. However, we reviewed the charts of and telephoned all patients we had not seen personally. This way recurrences which were diagnosed and treated by the other 12 providers in our group practice were included in the data. None of our index cases acknowledged getting medical care outside of our medical group during the six-month follow-up period. Thus, our recurrence estimates should include all medically attended illness. Recurrent cases occurring more than six months after the index case of otitis in a study patient are not included in this report.

Because we cannot precisely define the population at risk, we cannot make estimates of the incidence of otitis media in our area.

RESULTS

Otitis media was diagnosed, treated and followed for six months in 89 children. These children had 59 additional episodes within the six month follow-up period. Fifty-five percent of the cases were in

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males. Sixty-six percent of the children were under three years old, 84% under six and 92% under nine.

Hearing impairment occurred in five of 21 (24%) at the initial two week follow-up. Of these patients, three were referred for ENT evaluation and treatment and two others were subsequently found to have normal hearing.

Ninety-five percent of the cases had cleared and were normal by physical exam at two weeks. Ninety-seven percent were normal at three weeks.

Of the 89 children, 34 (38%) had a second case of otitis within six months, and 14 (41%) of these had a third case within six months of the first episode. Thirty-nine of 47 (81%) of the recurrences included the originally affected ear. Among males, 47% had a first recurrence and 52% of these had a second within the six month observation period. By contrast, only 27% of the female index cases had a recurrence and only 18% of these had a second recurrence in the six-month period. This is a significant difference between sexes ($p < .05$ by two-tailed test of difference between two proportions for first and second recurrences).

Patients cooperated by bringing back medicine bottles so that compliance in taking prescribed medicines could be estimated in 101 of 102 cases. Fifty-one percent (46 of 90) of compliant patients had recurrences within the six-month observation period. In contrast, only 9% (1 of 11) non-compliant patients had recurrences. This difference is statistically significant ($p < .05$ by two-tailed difference between two proportions).

DISCUSSION

Hearing impairment in our patients was less common than reported by others. Lowe⁴ in England, found 55% of children over four years old with otitis media had greater than 30db loss at six months. However, many of these patients were not treated with antibiotics and others were treated with tetracycline. Olmstead² found that 55% of children over two and a half years old with otitis had a transient loss, but only 12% had a permanent deficit beyond six months. Our finding of 24% impairment at two weeks is encouraging.

The vast majority of our patients clinically cleared their otitis within two weeks and all but 3% had cleared by three weeks. The Medical Research Council in England reports similar figures.⁵ Lowe⁴ found 29% not yet clear at four weeks. But, as mentioned above, many of these cases were not treated with antibiotics. And many of Lowe's patients did not report back. Since the well ones would presumably be preponderant in his non-reporters, Lowe's estimates of clearing rates are probably low.

We were surprised that over one-third of our patients had recurrent otitis, usually involving the same ear, within the six-month observation period.

But the Medical Research Council⁵ reports that over one-half of their cases of otitis media occur in children with a history of a previous episode. And others⁶ say about one-third of their cases recur within four months. The significantly increased susceptibility of males to recurrence is striking, but consistent with the general observation that young males are more vulnerable to disease than females. Because of these results, we plan to consider seriously prophylactic antibiotics⁷ for at least six months in males we see with otitis media.

Finally, the apparent protection from recurrence, which incomplete taking of the prescribed medicines seemed to afford, raises many questions. Others have found no difference between patients who take all their medicine and those who do not^{7,8} even though the criteria used was much less stringent (more than one-third of medicine remaining) that was ours. A delay in instituting antibiotics for bacterial otitis media may diminish the likelihood of recurrence or relapse,⁶ although why this is true is unclear. Conceivably, the discrepancies we note between these two groups of patients may in some way be related to the same phenomenon. On the other hand, we do not know what proportion of all cases of otitis seek medical attention. And if all do not, as we suspect, then some relatively non-compliant children could have suffered a recurrence at home without our knowing it.

In the future, we hope to examine long-term recurrence rates and hearing loss and the effect of decongestant therapy on the same parameters.

ACKNOWLEDGEMENTS

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Special Article

Medical Intelligence

DRUG THERAPY

Neurologic Syndromes Associated with Antipsychotic-Drug Use

Acute dystonias, akathisias and Parkinsonism have long been recognized as extrapyramidal side effects that occur in susceptible persons who are taking any of the drugs in the treatment of psychosis (Table I).^{*} These side effects often occur early in treatment, and they usually respond to dosage reduction or the addition of corrective medication. More recently, a quite different syndrome, tardive dyskinesia, has been found to be associated with antipsychotic drug use. Many aspects of the characteristics, etiology, prevention and treatment of this variegated set of symptom complexes are very unclear at present. However, patients who clearly show this syndrome are not uncommon, and the condition sometimes persists with little improvement for periods of one to two years or indefinitely.

The purpose of the present paper is to review our current knowledge about tardive dyskinesia and to contrast it with other neurologic conditions associated with antipsychotic drug use. We hope that this paper will help the practicing physician to diagnose these conditions and to decide what clinical practices are indicated.

In our opinion, the antipsychotic drugs are uniquely necessary to the effective treatment of

TABLE I

ANTIPSYCHOTIC AGENTS	
Commercial Name	Generic Name
Phenothiazines:	
Compazine	Prochlorperazine
Etrafon (Triavil)	Perphenazine and amitriptyline
Largon	Propiomazine
Levoprome*	Methotrimeprazine
Mellaril	Thioridazine
Phenergan	Promethazine
Proketazine	Carphenazine
Prolixin (Permitil)	Fluphenazine
Quide	Piperacetazine
Repoise	Butaperazine
Serentil	Mesoridazine
Sparine	Promazine
Stelazine	Trifluoperazine
Thorazine	Chlorpromazine
Tindal	Acetophenazine
Torecan	Thiethylperazine
Trilafon	Perphenazine
Vesprin	Triflupromazine
Butyrophenones:	
Haldol	Haloperidol
Innovar*	Droperidol
Thioxanthenes:	
Navane	Thiothixene
Taractan	Chlorprothixene

*Not marketed as an antipsychotic.

Prepared by the American College of Neuropsychopharmacology-Food and Drug Administration Task Force. Members of the Task Force are as follows: Burtrum C. Schiele, M.D., University of Minnesota Medical School; Donald Gallant, M.D., Tulane University Medical School; George Simpson, M.D., Rockland State Hospital, Orangeburg, N.Y.; Elmer A. Gardner, M.D., Division of Neuropharmacological Drug Products, Bureau of Drugs, Food and Drug Administration; and Jonathan O. Cole, M.D., Boston State Hospital. Consultants are as follows: George Crane, M.D., Spring Grove State Hospital, Baltimore, Md.; Frank Ayd, M.D., Baltimore, Md.; Jerome Levine, M.D., Psychopharmacology Branch, National Institute of Mental Health; Thomas Chase, M.D., Section on Experimental Therapeutics, National Institute of Mental Health; and Leszek Ochota, M.D., Bureau of Drugs, Food and Drug Administration.

*The term "antipsychotic drug" will be used in this paper in referring to these agents. This is now a more generally accepted and less confusing designation than other terminology such as neuroleptic, tranquilizer and ataraxic used more commonly in the past.

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schizophrenic illnesses. The limited information available on tardive dyskinesia, in particular, must be used with this fact in mind. Clearly to differentiate other drug-related extrapyramidal disorders from tardive dyskinesia, the other conditions are discussed first.

ACUTE DYSTONIC REACTION

Acute dystonic reactions are of sudden onset and consist of bizarre muscular spasms that have been misdiagnosed as tetany or hysteria. The muscles of the head and neck are predominantly affected, and the most commonly noted feature is an involuntary spasm of tongue and mouth muscles leading to difficulties in speaking and swallowing. The masseter muscles may be tightly contracted, so that the mouth cannot be opened. Facial grimacing may also be prominent. The neck muscles are also frequently affected; thus, opisthotonos, torticollis, etc., can occur and may be associated with oculogyric crisis

— i.e., spasm of the external ocular muscles with painful upward gaze persisting for minutes or hours. The back, arm and leg muscles are less frequently affected, but, when they are, they can produce bizarre gaits and difficulty in walking. The acute dystonic reactions usually take place within 24 to 48 hours from start of medication and occasionally occur or recur when there is an increase in dosage. Acute dystonic reactions occur more often in young people than in old, and in males than in females. The occurrence of this phenomenon appears to be a matter of individual sensitivity as well as of the dose and type of antipsychotic drug administered. These reactions are easily treated by parenteral administration of a wide variety of agents — e.g., antihistaminics, barbiturates, and anti-Parkinsonism agents. Response is dramatic, and continued medication is usually not required.

AKATHISIA

Akathisia refers to a subjective desire to be in constant motion rather than any specific motor pattern. Patients complain of an inability to sit or stand still, and of a drive to pace up and down. They may complain of being restless, fidgety and having to be in constant motion. The subjective feeling of muscle discomfort often precedes the onset of observable motor restlessness. Further subdivisions of this phenomena, such as *tasikinesia* or restless legs, are included in this category.

Akathisia may occur early in treatment and is sometimes mistaken for psychotic agitation; this clinical error can lead to an unnecessary further increase of the antipsychotic medication. The use of parenteral anti-Parkinsonism agents at this stage may produce an immediate response to the condition; however, it is not unusual for this type of extrapyramidal side effect to show an inadequate response to such medication, and it is frequently necessary to reduce the dosage of the antipsychotic medication or add a sedative agent such as diazepam or diphenhydramine. Treatment may then be continued with combined anti-Parkinsonism medication, and after a few weeks or months, the gradual withdrawal of this agent may be undertaken.

PARKINSONISM

This condition may be clinically indistinguishable from post-encephalitic or idiopathic Parkinsonism. It occurs at varying intervals after initiation of antipsychotic drug therapy at conventional dosage levels. Like the dystonias, it can be patient related or dose related. Thus, very high doses of medication can (but do not always) rapidly produce a picture resembling Parkinsonism. The signs are similar to those of the classic illness — i.e., the first signs are usually a reduction in facial movements followed by a reduction in arm movements, and ultimately the

shuffling gait, pill-rolling hand movements or other typical signs. Patients with fully developed cases have a generalized slowing of volitional movement, tremor at rest especially involving the distal upper extremities and rigidity, and treatment is by reduction of dosage or addition of conventional anti-Parkinsonism agents.

TARDIVE DYSKINESIA

Tardive dyskinesia, which has also been called "terminal extrapyramidal insufficiency," "complex dyskinesia" and "persistent dyskinesia," is a reasonably well defined clinical entity that can conceivably occur after several weeks or months of antipsychotic-drug treatment but is usually observed only after several years of treatment. In an unknown percentage of cases, the syndrome is apparently irreversible and can be called "permanent dyskinesia." Paradoxically, it may appear for the first time shortly after antipsychotic-drug treatment has been discontinued; antipsychotic agents can suppress the dyskinesia by inducing mild Parkinsonism. The incidence of the condition is almost impossible to state with any assurance since no clear criteria exist on which to base a diagnosis of minimal tardive dyskinesia and most reported prevalence surveys do not adequately define the population studied. It is rarely seen in acute psychiatric units, even in patients with recurring schizophrenia, and prevalence rates of the order of 20 per cent have been reported in older institutionalized patient groups with very chronic disease. Perhaps 3 to 6 per cent of patients in a mixed-psychiatric population receiving antipsychotic drugs would exhibit some aspects of this syndrome at one time or another. Symptoms overt enough to be recognized by a casual observer are not uncommon; severe and incapacitating symptoms are quite rare, fortunately.

The syndrome is more likely to be present in elderly patients and may well be more common in women and in patients with a prior history of brain damage.

A syndrome resembling tardive dyskinesia has been reported to occur in children receiving antipsychotic medication. In contrast to the adult syndrome, the mouth and face were rarely affected, and repetitive choreiform movements of the extremities were most common. In one published study, these movements disappeared over a one-year period in all 10 children studied. In an unpublished report, the syndrome disappeared completely within a month in half the 18 affected children. In both studies the syndrome was detected only after antipsychotic medication was stopped. There are informal reports of similar phenomena in adult psychiatric patients after only a few months of treatment. Again, the syndrome disappeared after a few weeks or months. It is unclear whether or not the above, more tran-

sient conditions should be called tardive dyskinesia.

Description

Tardive dyskinesia as usually seen in older patients with more chronic condition is characterized by stereotyped, repetitive, involuntary movements of the mouth, lips and tongue and is sometimes accompanied by choreiform movements of the limbs or trunk.

The most widely described symptoms make up the "buccolinguomasticatory" triad, which consists of sucking and smacking movements of the lips, lateral jaw movements, and puffing of the cheeks, with the tongue thrusting, rolling or making fly-catching movements. Such movements may be carried on with the mouth closed; the tongue hits the inside of the cheek, and a chewing-the-cud type of movement will be seen. Although the syndrome is the most frequently described and seen, it is by no means the only mode of onset. Sometimes tic-like movements involving the lips and eyes may antedate these symptoms, and other parts of syndrome, described below, may also appear first. The oral movements usually worsen under emotional tension; they disappear during sleep. It has been suggested, though not established, that fine vermicular movements of the tongue may be an early sign of tardive dyskinesia.

The extremities may show choreiform movements that are variable, purposeless, involuntary quick movements. They sometimes intensify on attention but are irregular in occurrence. Frequently associated with these symptoms are athetoid movements, which are continuous, arrhythmic, worm-like slow movements in the distal parts of the limbs. The choreoathetoid movements particularly affecting the arms and fingers are to be differentiated from schizophrenic stereotyped movements.

Another feature of the syndrome may be axial hyperkinesia — i.e., a to-and-fro clonic movement of the spine in the interior-posterior direction, a rare symptom, but one that has been seen as the only manifestation of the syndrome. Ballistic movements can also occur, as can rhythmical swaying movement of the body from one side to the other, which can take on a rocking quality if the patient sits down. All these features are seldom present at the same time, but the syndrome, in combination with choreoathetoid movements of the limbs and an inability to stand or sit still, is a frequent grouping of signs in severe cases. All involuntary movements disappear during sleep.

Symptoms of Parkinsonism can coexist with tardive dyskinesia.

Characteristic Features

Tardive dyskinesia should not be confused with

the acute dystonic reaction described above. To begin with, the tardive syndrome is characterized by a late onset, and the patient has usually received antipsychotic drugs for many years, often while chronically hospitalized. The manifestations may be masked by the antipsychotic drugs that the patient is taking and thus will only be seen if the drug is discontinued or the dosage markedly reduced. In many cases the tardive-dyskinesia will lessen or disappear, at least for a time, if large amounts of potent antipsychotic drugs are given to the patient, but this mode of therapy is not recommended lest a vicious circle occur. Persistence of the symptoms after the discontinuation of the medication is its most single characteristic manifestation; involuntary movements may persist for weeks or years and, in some patients, they may persist indefinitely. Moreover, full-blown cases of tardive dyskinesia may gradually subside if the antipsychotic drugs are discontinued, but other approved methods of successful therapy are so far lacking. Finally, in younger patients, and those whose symptom complex is less well developed, symptoms and signs may clear in relatively short periods after the discontinuation of antipsychotic agents.

Differential Diagnosis

Abnormal movement disorders occur in many patients who have never received antipsychotic drugs. Depending upon the type of onset, a differential diagnosis might include Sydenham's chorea, Huntington's chorea, congenital torsion dystonias, hysteria and the stereotyped behavior or mannerisms of schizophrenia.

Early Detection

The full-blown picture of tardive dyskinesia is easy to diagnose, but early cases are frequently missed. Possible early signs are the presence of tics in the facial region, ill defined abnormal mouth or eye movements, mild mouthing or chewing movements, the presence of rocking or swaying movements or the occurrence of reckless limb movements in the absence of the subjective discomfort associated with akathisia.

The temporary withdrawal of antipsychotic medication can be used as a way of detecting underlying early tardive dyskinesia.

Possible Etiology

Tardive dyskinesia resembles the abnormal movements seen with patients with Parkinsonism on L-dopa treatment and is suppressed by antipsychotic drugs, including the phenothiazines and haloperidol, which may block dopaminergic synapses, and by tetrabenazine and reserpine, which deplete the

Continued on Page 285



Putting out the fires of arthritic pain

Rheumatoid arthritis can sometimes spread like wildfire, with joint after joint going up inflamed: "The usual onset is manifested by spotty joint involvement but an acute onset of symmetrical polyarthritis may be noted."^{1,2}

If aspirin fails, consider Butazolidin alka. Giving one capsule four times a day often provides prompt, pain-relieving, anti-inflammatory action to help restore joint mobility. The results you can get within a week can be maintained on as little as one or two capsules daily.

Serious side effects can occur. Select patients carefully (particularly the elderly) and follow them closely in line with the drug's precautions, warnings, contraindications and adverse reactions. For full details, please read the prescribing information. It's summarized on the back of this page.

Butazolidin[®] alka


Each capsule contains:

100 mg. phenylbutazone USP

100 mg. dried aluminum hydroxide gel USP

150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.



**Fire fighter
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Butazolidin® alka

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If it doesn't work in a week, forget it.
Ragan, C.: The Clinical Picture of Rheumatoid Arthritis, in Arthritis, ed. 8, edited by J. L. Hollander and D. J. McCarty, Jr., Philadelphia, Lea & Febiger, 1972, chap. 21, p. 335.

Geigy

Important Note. This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Substitute alka capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia), dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications. Rheumatoid arthritis, osteoarthritis, bursitis, acute gouty arthritis and rheumatoid spondylitis.

Contraindications. Children 14 years or less, senile patients, history or symptoms of GI inflammation or ulceration including severe, recurrent or persistent dyspepsia, history or presence of drug allergy, blood dyscrasias, renal, hepatic or cardiac dysfunction, hypertension, thyroid disease, systemic edema, stomatitis and salivary gland enlargement due to the drug, polymyalgia rheumatica and temporal arteritis, patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings. Age, weight, dosage, duration of therapy, existence of concomitant diseases and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and GI tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions. The following should be accomplished at regular intervals. Careful detailed history for disease being treated and detection of earliest signs of adverse reactions, complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions. This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult GI bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult GI bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, convulsional states, lethargy. CNS reactions associated with overdosage including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia, ulcerative stomatitis, salivary gland enlargement.

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brain of dopamine. It is therefore possible that tardive dyskinesia is related in some way to excessive dopaminergic activity in the brain.

Treatment

Agents effective against Parkinsonism do not relieve tardive dyskinesia and may aggravate it. Since tardive dyskinesia is presumably a result of treatment with antipsychotic drugs, it seems reasonable to withdraw such drugs entirely once the condition is diagnosed. On the other hand, with current lack of information it is impossible to tell whether or not continued antipsychotic medication will aggravate the condition. In the rare, very severe cases with mouth lesions or respiratory symptoms, an antipsychotic drug may have to be used to relieve the patient's distress.

In patients with chronic dyskinesia whose clinical state remains stable without antipsychotic drugs, complete withdrawal is indicated. In those whose psychosis worsens when these drugs are removed, a clinical choice between two evils must be made. The use of the lowest possible dose of antipsychotic drug adequate to control psychotic symptoms appears to be the best approach. In the absence of any real data indicating that a particular antipsychotic drug is more likely to be associated with tardive dyskinesia than any other, a patient with tardive dyskinesia needing such a drug might well be given the drug least like the one on which dyskinesia emerged. The use of sedative or antianxiety drugs may occasionally enable the clinician to avoid resorting to an antipsychotic agent.

Although some patients show little or no improvement in the dyskinesia even after months or years of drug withdrawal or minimal antipsychotic use, the condition does not usually progress in severity and

some patients gradually improve or recover completely.

Prevention

Because of the lack of adequate substitutes for the antipsychotic drugs in the treatment of psychosis, tardive dyskinesia has been accepted as an undesirable but occasionally unavoidable price to be paid for the benefits of prolonged antipsychotic drug therapy. However, the physician may be able to reduce the risk of this syndrome in several ways. For example, he can minimize the unnecessary use of antipsychotic medication (especially at high doses) in long-term patients. Many patients with chronic psychosis can be satisfactorily maintained for long periods without antipsychotic drugs. Drug holidays in patients receiving long-term medication are advised for a number of reasons. First of all, and most importantly, they allow the doctor to ascertain whether or not there is evidence of tardive dyskinesia. If the patient presents these symptoms, every effort should be made to treat him without the use of antipsychotic drugs. Secondly, the occasional discontinuation of the drug may afford a small amount of protection from the long-term hazards of these otherwise very useful agents.

If possible, antipsychotic drugs should be discontinued at the first sign of abnormal oral movements or other manifestations of tardive dyskinesia.

These precautions should be carefully observed in the elderly (women especially) and probably in all patients over 50 years of age.

It should be recognized that the above recommendations have evolved in the absence of any clear evidence that tardive dyskinesia is specifically related to any particular drug, dosage level or dosage duration.

Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The bylaws of the Maine Medical Association were amended in June of 1973 as follows: Chapter I, Section 11, — "Each member of the Maine Medical Association shall be required to report his activities in continuing medical education every year according to a format provided by the Committee on Continuing Medical Education."

Only active, dues-paying members are required to report this year.

Please fill in your activity report promptly and return to the M.M.A. office, P.O. Box 250, Brunswick, Maine 04011.

Planning a Rural Community Health Center*

FRANK A. HALE, Ph.D.,** ARTHUR R. JACOBS, M.D., M.P.H.†
and DALE GEPHART, M.D.‡

ABSTRACT

Among the most controversial policy issues confronting health planners is the role of the small, under-utilized rural hospital. Planning agencies have urged a medical care *system* which integrates resources from multiple communities into a regional organization for purposes of improving services while reducing costs. This approach may provoke confrontation with the community hospital advocates, who contend that locally accessible, acute care services are not necessarily more costly or of inferior quality and can be more responsive to consumer demand.

The tension between town and region is clearly seen in the case of a Northern New England rural community where an obsolete hospital was recently replaced by a modern facility in spite of opposition by planning groups.

While the community rejected regional planning objectives in favor of a local strategy to meet its perceived immediate need for a hospital facility, the tension between local and regional interests produced a dividend, for it led to the creation of a more flexible responsive facility and health care team, able to offer a broad array of services. The new hospital and health clinic is probably quite different today than when originally conceived. The process by which it evolved exemplifies the political nature of health resource planning.

INTRODUCTION

American suspicion of the centralization of

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power, especially when it is vested in governmental agencies, is deep and pervasive. The Jeffersonian tenet: "That government is best which governs least," has traditionally influenced Americans' attitudes and beliefs toward their health care system. In recent times, as the advance of medical technology has accelerated and consumer expectations and aspirations with respect to what the health care system can and should provide have risen sharply, pressures for coordination and integration of health resources—for more government—have mounted. Other factors including increased expenditures for health care, especially hospital care, population growth, longer life expectancy, migration from rural to urban areas, and expansion of the numbers and variety of health care professionals and organizations, have provided further impetus to increased public sector involvement in the organization, financing, and delivery of health care.

The Comprehensive Health Planning and Regional Medical Program legislation enacted by Congress in 1966 are evidence of the strength of these pressures. These Public Laws have promoted the development of government subsidized health planning agencies and research programs charged with defining area health problems, selecting priorities, and, in the light of these, coordinating the various attempts to meet health needs. Since hospital care is the most visible and costly health resource, much of the planning and research to date has focused on the hospital (Klarman, 1964; Neuhauser and Turcotte, 1972). The role of the small rural hospital facility is one of the most difficult policy issues currently confronting health care planners (Robinette, 1972; Somers 1971).

Areawide planning agencies tend to support the concept of a medical care *system* in which regional resources are integrated in order to improve the quality of health and medical care services while at the same time reducing costs to both providers and consumers through economies of scale. As one "Regionalist" who participated in the events reported in this paper remarked:

Only through this kind of coordination and consolidation can we recruit and retain skilled medical personnel, only in combination can we muster the financial resources to take advantage of technological systems and equipment now needed for acute care. And only in this manner can we command and benefit from

TABLE 1

ADJACENT AREA TOWNS AND HOSPITALS (NON-FEDERAL)			
	<i>Estimated Patient Shed</i>	<i>Distance From Community</i>	<i>Hospital Beds</i>
Town A	24,981	16 miles	86
Town B	22,579	36 miles	70
Town C	39,060	10 miles	84
Town D	Referral Center	19 miles	362
Town E	10,208	20 miles	27

close and mutually rewarding relationships to medical school centers and referral hospitals.

The regional approach may lead to confrontation with the community hospital advocates who are often active and vocal at the grass roots level. This group contends that locally accessible, familiar and personal services are more responsive to consumer demand and not necessarily more costly or of inferior quality. Moreover, it is argued that a hospital attracts new physicians to the community and is a source of employment for area residents.

The tension between town and region can become especially salient when a community faces the prospect of losing its existing hospital and must choose among such alternatives as replacing it, modifying its present service patterns, or even abolishing it.

This paper reports on a rural community in Northern New England which recently faced just such a crisis when the local hospital, (an obsolete, thirty-bed, wooden frame structure built in Civil War times), was denied State accreditation and became ineligible for Hill-Burton hospital construction funds. The decision-making process which led to the creation of a modern community health center and acute care facility despite opposition by regional planning groups illustrates a number of political issues surrounding the planning of health care systems and highlights some strengths and weaknesses of the regional planning process.

BACKGROUND AND SETTING: THE COMMUNITY AND THE HOSPITAL

The Community dates from pre-revolutionary times and throughout the nineteenth century was a leading regional center for small industry. The town census has varied little in the last century. In 1970, the population was 4,158. Current major sources of employment are a state prison, a machine tool factory, and a rubber products factory. The latter two each employ about 950 workers. Several neighboring communities contribute to the labor force and patronize local merchants. Patients' utilization patterns are difficult to estimate. The Hospital is one of several in the region. (Table 1) The local Comprehensive Health planning agency has estimated its patient shed at about 15,000.

A comparison of state, county, and town data with respect to family income (Table 2) shows that

TABLE 2

	AREA INCOME DATA*			
	<i>Town</i>	<i>County</i>	<i>State</i>	<i>United States</i>
Median Family Income	9,531	9,322	8,929	10,474
% of Family Incomes Below Poverty Level	5.4%	7.3%	9.1%	8.5%

*based on 1969 figures

Source: United States Department of Commerce 1970 Census Report

the community is relatively affluent for the region. The county in which it is located is, in fact, second highest among the State's counties in median family income. Also, while 7.3% of families in the county have annual incomes below the federally defined poverty level, the figure is lower for the community (5.4%).

In 1934, an old residence in the center of town was converted for use as a thirty-bed hospital. For the next twenty years, the facility and the four to six active physicians were able to meet the needs of the area quite well. With generous financial assistance provided by private patrons to maintain the structure, purchase equipment, and pay part of the overhead, the facility managed to serve the community for over thirty years. However, in the late sixties it became apparent that the building was obsolete when compared to modern health facilities. Fire and safety features were marginal and under the 1970 State Licensing Standards the institution would lose its accreditation.

Statistical reports began to reveal a decline in the utilization of the facility. A 1969 study by the area planning agency reported that the occupancy rate at the hospital dropped from 58.1% in 1963 to 56.7% in 1968, a decline of 2.4%. The decrease would have been greater had not the length of stay increased from 6.4 days to 9.1 days, an increase of over 40%. As Table 3 shows, both of these indicators compared unfavorably with national and regional trends. The study concluded that patients were shifting to the two nearby larger area hospitals. The study also pointed out that the cost of hospitalization at the community hospital increased at twice the national rate for that time period.

The medical staff of the hospital had been depleted in the sixties so that only two full-time physicians remained. Obstetrical services were abandoned. A pathologist and a radiologist were available only on a shared time basis and one of the physicians continued to perform surgery. The emergency room, functioning under the supervision of a part-time nurse-director, was often the only primary care available in town. At the same time, it was believed that without an adequate acute care facility, the likelihood of attracting young physicians was diminished. The Board of Trustees were presented with a real dilemma as they sought to develop policy.

TABLE 3

	UNITED STATES			THE PLANNING REGION HOSPITALS			THE COMMUNITY HOSPITAL		
	1963	1968	% CHANGE	1963	1968	% CHANGE	1963	1968	% CHANGE
Occupancy Rate (%)	76.0	78.2	+ 2.89	68.9	69.9	+ 1.5	58.1	56.7	- 2.4
Length of Stay (Days)	7.7	8.4	+ 9.09	7.21	8.51	+ 18.03	6.4	9.1	+ 42.18

Source: Derived from data reported in the local Comprehensive Health Planning Agency Document: *Community Report on Health and Medical Care Resources*, December 1969.

Thus, as the decade of the sixties drew to a close, the community faced two immediate problems: a critical need for physicians and a health care facility that badly needed replacement. The question of whether or not the hospital should be attempting to fulfill the role of an acute care facility began to receive increased attention.

REGIONAL PLANNING EFFORTS

About the same time the hospital issue was becoming significant in the community, the regional planning movement began to gather momentum. During this period, two agencies were created with the goal of regionalizing health care in the area: an area-wide Health Planning Agency, cited above; and a private Regional Health Council.

The Planning Agency was organized after a series of meetings in 1967 among representatives of the region's hospitals to talk over mutual concerns. Believing that a broad approach to health care problems was needed, representatives of this group consulted both the State Hospital Association and the Regional Medical Program. The Regional Medical Program encouraged the implementation of a study to inventory the health resources of the area as a start toward the regionalization of health care and agreed to partially fund this effort as a pilot project until Comprehensive Health Planning Act funds could be obtained.

In the spring of 1968, the area-wide Health Planning Agency was incorporated under the laws of the State. All six hospitals in the immediate area were charter members. The organization has also sought to work with and include non-hospital health oriented organizations and agencies. A major expressed goal of the agency is the "... development of a sound masterplan for improved and more unified health care throughout the region. . . ." A New England Regional Commission grant assured the completion of an *Inventory of Health and Medical Care Resources* which was published in 1969 to be used as a planning resource for other health agencies.

The Regional Health Council was formed in 1970 as a result of the data collection efforts of the Planning Agency. Its objective was the creation of a regional acute care hospital which would serve the patient sheds of five of the small community hospitals providing services to forty-one adjacent towns containing a population of over 77,000 people. Two of the five local hospitals provided \$10,000 each as

"seed money" for this effort. It seems evident that trustees from each expected that the regional referral hospital then being contemplated would be placed within or near their own town borders. The New England Regional Commission also assisted this project through a \$25,000 grant. These resources were applied to proposal development and led to the Council receiving, as of July 1971, a grant of \$167,000 from the Department of Health, Education, and Welfare to develop a health maintenance organization. The group premised its activities on the belief that none of the five small acute care hospitals could be expected to provide a complete range of acute care skills. Thus, their continued existence represented a duplication of resources which led to competition rather than integration and resulted in an inefficient and more expensive health delivery system. What was their prescription for the situation? A July 1971 press release offered an answer:

It is our suggestion that the five present community hospitals focus specifically on the delivery of ambulatory health care and social services — outpatient care and treatment from primary physicians and their skilled assistants and a full complement of health education clinics and counselling, all based there.

We propose that a broad-based health facilities corporation be charged with the responsibility for conversion of the present hospitals to Community Health Centers and the development and construction of a new acute care hospital.

While the Council and Health Planning Agency both assumed a regional focus, each had a distinct orientation. Whereas the planning group inventoried resources in the existing health care system, the Health Council began to lay the groundwork to change the system through regionalizing its health delivery mechanisms.

THE COMMUNITY RESPONSE

The Trustees of the Hospital were not responsive to the Health Council proposal to create a regional referral hospital. They had strong evidence that their community would not support the creation of a facility limited to outpatient care. When it had become apparent that the old hospital would have to close, the Trustees began studying what options were available. Surveys indicated that the most the community would be able to raise would be

\$250,000; consequently, outside financial assistance would be necessary if a new ambulatory or acute care facility were to be constructed. In a background statement prepared by the Community Hospital's Trustees for the Planning Agency Review, their rationale is clearly set forth:

The Trustees discovered that although Hill-Burton funds for hospital construction were not available for (the community), some financial aid could be made available for the erection of a health clinic. An architect was engaged to prepare preliminary studies of a clinic with attached nursing home wing. Public reaction to this move was immediately made evident and was strongly adverse. The two large industries upon which the general economy of the community depends and which have annually been significant contributors to the hospital both in terms of financial aid and in terms of patients served, announced that they would give no support to any new building unless it included acute care facilities. Similar opposition was voiced by the community generally.

Recognizing that without the support of industry and of the public, the proposed health clinic was doomed to failure, the Trustees again sought ways to provide a hospital facility. A lease proposal made by (a private group) appeared to offer the best opportunities and after much negotiating and analysis, a lease was signed with this firm for the construction of the Hospital and Health Center.

According to the terms of the lease agreement, the Hospital Corporation agreed to lease the facility for a period of fifteen years. At the end of that time, the Corporation must purchase the Hospital for an already agreed upon sum. This arrangement has made it possible for the Community to have its hospital without having to make a high capital investment which it could not have afforded.

In July 1970, a community drive to raise funds for a new hospital was launched. Apparently no strong attempts to involve planners at either the regional or state level were made at this time. Community support, however, was enthusiastic. For example, some local business executives spent a great deal of time assisting the Trustees in their fund-raising activities. By the Spring of 1971, over a half million dollars had been raised from nearly 1600 subscribers. A portion of this money was placed in escrow to be used at the end of the lease to purchase the facility.

The viewpoint of industry is not difficult to understand since a local hospital is an attraction to potential employees as well as an advantage in case of plant emergencies. Indeed, one of the large firms in the community paid for the Emergency Room. The fact that there appears to have been widespread

community support is more complex and difficult to explain, especially given the fact that there had been a trend toward seeking medical care outside the community and that the level of community spirit seemed to be low; for example, a number of stores on Main Street were empty at this time. A number of individuals including Hospital Trustees, area physicians, Council and health planning officials, and community leaders, have indicated during interviews several factors which seem to explain the community viewpoint:

1. The presence and influence of two highly regarded physicians who had served the community for three decades and who wanted to see a hospital continued there.
2. The feeling on the part of the community leaders that without a complete acute care facility it would be extremely difficult to attract new physicians to the area.
3. The plans of the Board of Trustees which appeared to be aimed at the creation of an extremely flexible facility which would meet a wide range of community health needs.
4. The availability of land (donated by the state) and a financial mechanism to construct a facility and pay for it over time.
5. A feeling of resentment toward "outsiders" who had recommended a lesser facility in the interests of regional health care or area health planning.

THE REGIONAL REACTION

When it became apparent to the Health Planning Agencies that the community was going to proceed with a *hospital* construction program, they spoke out against it. In its "Report to the Trustees" dated July 26, 1971, the Regional Council urged the community: "to negotiate a more flexible plan to meet its local needs and simultaneously benefit from area-wide developments." The report concluded:

It is our strong belief, expressed with considerable confidence and backed by guidelines which have regional, state and national endorsement, that five years from now, community residents will be served most effectively and economically by an area-wide system of health and medical care which concentrates acute care in a single regional facility and delivers ambulatory primary, and chronic care from small town and rural health centers.

The Regional Medical Program also expressed substantial misgivings with regard to the hospital project as highlighted by the following statements about the community:

The hospital was declared ineligible for Hill-Burton funds. However, private funding was obtained. After the decision had been made to build the hospital, Blue Cross asked the state

Comprehensive Health Planning Agency to make a report on whether the hospital should be built. Regional Medical Program data contained in the ensuing report indicated that if the hospital were built the area likely would become the most expensive hospital area in the state on a per capita basis because many hospitals in the area already had low occupancy rates. Doubt was also expressed that the hospital could attract enough physicians to run it. Nevertheless, — the hospital is being built and it is doubtful that Blue Cross will be able to withhold support.

Perhaps the clearest indication of regional frustrations with the community's health planning efforts is seen in the meeting of the Review Board appointed by the Comprehensive Health Planning Agency which, under the law, was charged with developing an official review mechanism for the hospital and health center proposal. The Agency had already documented trends which seemed to indicate that patients were inclined to go out of the local area to receive medical services. Yet the review appears to have been a *pro forma* exercise; it even occurred after construction began. The minutes of the Review Board Meeting point out the dilemma facing regional health planners who must deal with resolute local communities.

The members of the Review Board were unanimous in their opinion that they had been placed in a most awkward position. Ideally, the review process should take place under circumstances which allow a useful purpose for the review. The situation the Committee encountered was one in which a community had already begun implementation of plans for a health facility. . . . The problem in reviewing this proposal had its origin in the lack of an official review mechanism at the time of planning this facility some two years ago. At this point in time, reconsideration of plans either for construction or for financing is impossible. . . . It is difficult to describe precisely the acute discomfort felt by the members of the Review Committee in attempting to review a project, which despite its intrinsic value, had already been enthusiastically supported by a community of some 7,000 people.

The Review Committee appears to have recognized the dilemma of the local Board of Trustees as they sought to balance their immediate needs against the long-range needs of the Region:

In our discussion with the representative of the Board of Trustees of the hospital, we noted that they were anxious to meet what they had perceived as their immediate needs for this community and could not realistically delay meeting these needs until such time as the Council

had planned and implemented its broad program. We also noted that the representatives of the Board of Trustees were quite amenable to altering the function of their facility, that is, in diminishing the acute care component if the subsequent development of the health care system in the regional planning area would make this alteration feasible.

Throughout the planning, the Trustees had concerned themselves with creating an institution both flexible and able to respond to a broad range of community health needs. Thus, the hospital and health center which evolved and began providing services in the Fall of 1972, offered several levels of care under one roof. Included are the following:

1. An acute care facility with thirty beds, a surgical area, and radiology and laboratory facilities.
2. An emergency department.
3. A thirty-bed nursing home for extended care patients.
4. A wing devoted to outpatient facilities with office suites for the doctors, administrative and secretarial space, offices for the local home health agency, mental health programs, and community groups, and a possible dental suite.

CHANGES IN HEALTH CARE PATTERNS: THE FIRST YEAR

Despite the pessimistic predictions of the regional agencies, the hospital and health center appears to be fulfilling many of the goals of its supporters. The impact of the new facility is especially evident with respect to health manpower.

It was pointed out earlier that the doctor shortage was considered by some in the community to be a more significant problem than the availability of conforming hospital beds. This group tended to see the principal purpose of a new institution as attracting and maintaining professionals in the community. In their statement to the Review Board, the Board of Trustees noted:

The community has experienced as have many others in the country, difficulty in securing an adequate number of doctors. In this age of specialization, general practitioners are woefully scarce. Candidates for supplementing the group of physicians have been quite frank in stating that the close-to-obsolete hospital has been the major factor which has discouraged them from joining the community. Although it is acknowledged that a new building will not in itself automatically solve the problem of obtaining additional doctors, it will certainly enhance the possibilities for a solution.

Since the new facility began operating, the number of physicians serving the population has in-

creased from two to five. Two have come largely due to the assistance of The Department of Community Medicine at a nearby Medical School. The Trustees, worried about the predicted failures of the new facility requested assistance from the Department of Community Medicine in obtaining new physicians. Even before the building was completed, an internist with leadership qualities and a firm commitment to integrated community care had been recruited. He was joined later on by a pediatrician in the National Health Service Corps. The negotiation and selection process with respect to these two young and innovative individuals has broadened the Trustees' concept of the role of the primary care physician. The most recent arrival is a general surgeon.

All five physicians now have their offices at the new hospital and health center. In addition, physicians from nearby communities, some of whom are specialists, regularly visit the facility. There is also a MEDEX physician's assistant. Finally, it appears that other health agencies such as the local Visiting Nurse Association and Community Mental Health Group are starting to use the hospital as a base of operation.

Inpatient bed utilization statistics for the 30 acute care and 28 nursing home beds at the new hospital indicate that the occupancy rate for acute care beds averaged slightly less than 50% in the first ten months of operation. Thus, as the regional planning groups had predicted, utilization patterns did not change from what they were in the old hospital. Hospital officials believe that admissions would be higher if another physician were to serve the area. Occupancy rates among the nursing home beds are much higher, probably because the age distribution of the population is skewed toward the elderly and also because there is a scarcity of extended care facilities in the region. As of March 1, 1973, eight more nursing home beds were licensed at the health center.

DISCUSSION

The most crucial issues in health planning relate to control over the development and operation of the system. Centralized and coordinated health systems can occur only at the expense of local political and administrative autonomy. The planning and construction of the community hospital and health center went forward as a community enterprise in spite of pressure exerted by regional plan-

ning agencies. The inability of these groups to alter the community's plans to conform to the long range regional approach testifies to the pluralist nature of the health planning process in Northern New England. Indeed, the Health Council's own efforts to plan and organize an innovative health care delivery system for the region have not succeeded. The Agency was dissolved in August 1973 when its Federal program funds were suspended and it became clear that it had failed to generate the necessary grass roots constituency to operate from a community and regional base.

While the community rejected regional planning objectives in favor of a local strategy to meet its perceived immediate need for a hospital facility, the tension between local and regional interests produced a dividend, for it led to the creation of a more flexible responsive facility and health care team, able to offer a broad array of services. The new hospital and health clinic is probably quite different today than when originally conceived. The process by which it evolved exemplifies the political nature of health resource planning.

The fact that the Trustees sought out the local medical school as an alternative planning resource to the community further reinforces a major conclusion, namely, that when faced with threatened external control of local resources by regional interests, communities are likely to respond by seeking ways to preserve their capacity to self-govern. In so doing, they reflect deeply held, long established beliefs about centralization of power in the United States. The trend toward Certificate of Need Legislation at the State level, and the strengthening of review mechanisms in the 1972 Social Security Amendments are indicators that the issues posed by the clash of regional and local interests with respect to health planning will continue and even intensify.

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Maine Blue Cross and Blue Shield News

HEALTH EDUCATION ROLE

Maine Blue Cross and Blue Shield is becoming increasingly involved in the health education field, both through a fine series of booklets and films from Blue Cross Association and National Association of Blue Shield Plans, and through cooperation from public and commercial television stations, and health educators.

The Blue Cross Association and National Association of Blue Shield Plans booklets and films offerings have been a regular part of the Maine Blue Cross and Blue Shield effort for a number of years. Only recently with our entrance into the Maine Health Education Consortium, the Maine Health Education Cooperative Association, and increased communications about them, have they received the attention of health educators through which they will get broader distribution and more controlled utilization.

Beyond these efforts, Maine Blue Cross and Blue Shield has also sponsored health education programs. We have supported "Inside/Out," an in-school video mental health educational series for 8 to 10-year olds designed to help children understand the strains of growing up and thus lead healthy lives.

"Self, Inc.," which will be coming out soon, is a similar series designed for older children which we have also supported. Both "Inside/Out" and "Self, Inc." were brought into the State through the Maine Health Education Consortium, of which we are a member organization.

"Feeling Good," the best known public television health education program, has received Maine Blue Cross and Blue Shield support since its inception. It is now hosted by Dick Cavett and airs Wednesday night.

We have also sponsored a variety of other health education programs. Last fall, we ran a series of ten one-minute ads for children featuring Mr. Rogers. The ads warned children of various health hazards they might encounter. The ten ads were incorporated into a booklet which is presently the most popular item in our health education library.

Our sponsorships to date have also included alcoholism films, the "Medix" series (still running), and two Readers Digest films, "I am Joe's Heart" and "I am Joe's Spine."

Why Bother?

We advertise to try to help the enrollment effort and to broaden the public understanding of Maine Blue Cross and Blue Shield. We have involved advertising money in health education for a different reason. We realize our responsibility to our subscribers to operate efficiently, but through health education we are also saying that the consumer has a responsibility.

The consumer of health care services has the responsibility, to himself and the system from which he receives health services, to take care of his own health to a reasonable extent. That is, he should become educated about the factors that affect his health and ways he can help stay healthy. Our educational efforts are meant to help the consumer reach a level of knowledge whereby he can adequately take on part of the responsibility for his health.

A Maine Blue Cross and Blue Shield hypothesis has evolved which says simply that any efforts which help an individual to take more responsibility for his own health will lessen the load on acute care facilities and allow us to expand our efforts into more ambulatory services, ergo our strengthened health education role.



Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

- Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
- Can relieve nausea and vomiting often associated with vertigo.*
- Usual adult dosage for Antivert/25 for vertigo*: one tablet t.i.d.
- Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
- Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION:

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG 
A Division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert[®]/25 (meclizine HCl) 25 mg. Tablets for vertigo*

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

main purpose of drug information for the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with this agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a long one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

*

WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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Necrologies

PHILIP PINES, M.D. 1914-1975

Dr. Philip Pines, 60, of Limestone, Maine, died unexpectedly on March 18 in Miami, Florida while visiting there.

Born in Poland on June 13, 1914, he was the son of Bernarde Pines.

Dr. Pines received his medical degree from the University of Basel, Switzerland in 1940, interned there and served residencies at the St. Clare Hospital and University Hospital in Basel, and the Maryland Washington County Hospital in Maryland.

Dr. Pines practiced in Switzerland from 1946 to 1948 and located in Limestone in 1952.

He was a veteran of the Korean Conflict and was a Captain in the USAF(R).

Dr. Pines was a member of the Aroostook County Medical Society, the Maine Medical Association and the American Medical Association. He was also a member of the American Society of Abdominal Surgery and the International College of Surgeons.

Surviving are his widow, Susan Pines of Limestone; a son, Philip J. of West Medford, Massachusetts; and a daughter, Mrs. Brian Braisendell of West Scarborough.

RALPH L. REYNOLDS, M.D. 1883-1975

Dr. Ralph L. Reynolds, 92, of Waterville, Maine, died on April 12.

He was born in China, Maine on January 7, 1883, son of Franklin B. and Mary Anne Reynolds.

Dr. Reynolds received his college education at Colby College where he was graduated in 1906, and was a member of the championship baseball team, captained by "Colby Jack Coombs." He remained an ardent baseball follower throughout his years.

In 1913, Dr. Reynolds received his medical degree from Harvard Medical School, interned at the Boston City Hospital, served a residency at the Boston Lying-In Hospital and was a Graduate Assistant there for one year. He established practice in

Waterville in 1915 and practiced actively until mid-1974 when illness forced his retirement.

An honorary member and past president of the Kennebec County Medical Association, and the Maine Medical Association, Dr. Reynolds received a 50-year pin in 1963, a 55-year pin in 1968 and a 60-year pin in 1973. He was also a member of the American Medical Association, the American College of Surgeons, the Boylston Medical Society of Harvard Medical School, and was a Charter Member of the New England and Maine Obstetrical and Gynecological Society.

Surviving are a son, Dr. John F. Reynolds of Waterville; a daughter, Mrs. Philip Livingstone of Winchester, Massachusetts; and six grandchildren.

DACOSTA F. BENNET, M.D. 1885-1975

Dr. DaCosta F. Bennet, 89, of Lubec, Maine, died on April 27 in Manchester, New Hampshire.

Born in Lubec, Maine on June 4, 1885, he was the son of Eben H. and Anne W. Bennet.

Dr. Bennet was graduated from the University of Maine and received his medical degree from the University of Maryland School of Medicine in 1917. He did postgraduate work at the New York Lying-In Hospital and Penniman Hospital in Virginia. Dr. Bennet practiced in Penniman for one year and then

located in Lubec in 1919.

An honorary member of the Washington County Medical Society and the Maine Medical Association, he received a 50-year pin in 1967 and a 55-year pin in 1972. Dr. Bennet was also a member of the American Medical Association.

Surviving are two sisters, Mrs. Clarence Watts of Windber, Pennsylvania and Mrs. Ralph Preble of Cape Elizabeth; two sons, Dr. Eben T. Bennet of Cape Elizabeth and Frank Bennet of Manchester, New Hampshire; and six grandchildren.

OTIS J. DOUPHINETT, M.D. 1901-1975

Dr. Otis J. Douphinett, 74, of Scarborough, Maine, died unexpectedly on June 21 at a local hospital after a short illness.

He was born in Franklin, New Hampshire on May 16, 1901, son of Charles E. and Mary L. Douphinett.

Dr. Douphinett was graduated from Tufts University and received his medical degree from Tufts University School of Medicine in 1926. He interned at the Norwegian Hospital in Brooklyn, New York and served a residency at the Brooklyn Eye and Ear Hospital. In 1932, Dr. Douphinett located in Portland.

He was a senior member of the Cumberland County Medical

Society, the Maine Medical Association and the American Medical Association. Dr. Douphinett was a staff member of the Maine Medical Center and Mercy Hospital, as well as a former Chief of Ophthalmology.

Surviving are his widow, the former Margaret E. Smith; two sons, John O. and Paul, both of Scarborough; two daughters, Misses Mary Louise Douphinett of Burlington, Vermont and Jeanine Douphinett of Scarborough; a sister, Mrs. Thelma Duncan of Franklin, New Hampshire; and several nieces and nephews.

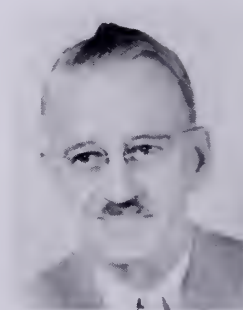
CHARLES N. STANHOPE, M.D. 1889-1975

Dr. Charles N. Stanhope, 85, of Dover-Foxcroft, Maine, died on April 30, following a long illness.

Born in Charleston, Maine on June 21, 1889, he was the son of Dr. Alvin H. and Martha Ella Stanhope.

Dr. Stanhope was graduated from Foxcroft Academy in 1907, taught school in Onawa and Addison before entering Bates College from which he was graduated in 1912. He then taught at Sangerville High School for two years before entering Bowdoin Medical School, where he received his medical degree in 1918. From January 1918 to August 1918, he served as Assistant Superintendent at the Western Maine Sanatorium and then located in Dover-Foxcroft. Dr. Stanhope specialized in the field of Public Health and was affiliated with the State Department of Health from 1936 to 1959, and was special consultant there until 1969 when he retired.

He was an honorary member of the Piscataquis County Medical Society and the Maine Medical Association, receiving a 50-year pin in 1968 and a 55-year pin in 1973. Dr. Stanhope was also a member of the American Medical Association and a



member of the staff of the Mayo Memorial Hospital.

Surviving are his widow, Maude Stanhope; one son, Murray M. Stanhope of Dover-Foxcroft; one daughter, Barbara M. of Providence, Rhode Island; four grandchildren; two great-grandchildren and several nieces and nephews.

RONALD A. BETTLE, M.D. 1914-1975

Dr. Ronald A. Bettie, 60, a well-known Brunswick, Maine practicing surgeon and a founder of the Parkview Memorial Hospital in 1959, died on July 8 of injuries sustained in a car crash in Bellemead, Montgomery Township, New Jersey. Dr. Bettie was working at the new Seventh Day Adventist Hospital in Hackettstown, New Jersey in an attempt to strengthen the hospital and staff, when the accident occurred. He had planned to return to Brunswick in the summer of 1976 to continue his private practice and association with the local hospital.

Born in St. John, New Brunswick, Canada on August 1, 1914, he was the son of Mr. and Mrs. Daniel K. Bettie.

He was graduated from Southern California Junior College in Arlington, California in 1935 and received his medical degree from the College of Medical Evangelists in 1939. Dr. Bettie interned at the Hackensack Hospital in New Jersey, served four

years in the U.S. Army as a Major, served a residency at the Maine General Hospital in Portland, Maine and then located in Brunswick in 1949. Several years ago, Dr. Bettie traveled to Kenya, Africa in response to a need for a temporary surgeon for one year. His son, Daniel, is a Seventh Day Adventist Missionary in Zaire, Africa.

Dr. Bettie was a member of the Cumberland County Medical Society, the Maine Medical Association and the American Board of Surgery.

Surviving are his widow, Ruth Bettie; his mother and father of Pennellville Road in Brunswick; three daughters, Jean Fuleki of Welland, Ontario, Ruth Harms of Kennewick, Washington and Jan Ellis of Bowdoin; a son, Daniel Bettie of Zaire, Africa and two sisters, Donna Kuczma of Barre, Massachusetts and Lois Ponte of Clinton, Massachusetts.

IN MEMORIAM

The first time I ever *heard* of Dr. Bettie was 5 months after I had arrived in Brunswick. There was a notice in the paper that Dr. Ronald Bettie would soon begin to practice here. I was struggling to build a practice, and he represented competition. I was, to put it mildly, dismayed. I needn't have been.

The first time I ever *saw* Dr. Bettie was shortly after he arrived. He made it a point to visit the other physicians and make himself known (an excellent example of his ability to get along with people) and to point out that he was not competition but cooperation.

For the next twenty-six years, our lives intertwined like streamers at a party. We saw each other professionally and socially. He delivered one of my children. I attended the weddings of his children; he attended the weddings of mine.

Professionally he was a skilled diagnostician and a remarkable technician. Let me give you just one example of his surgical ability. There are, of course, hundreds of others, but this one sticks in my mind. Shortly after Dr. Bettie had arrived in Brunswick, I saw a patient with cancer of the ovary. In those days, most of the major surgery was done in Portland. Dr. Bettie performed the surgery on this patient at the old Brunswick Community Hospital. The patient is still alive today, 26 years later. What better tribute to his judgment and surgical ability!

I remember vividly the long talks we used to have while scrubbing for surgery and over the surgical table where I assisted him many, many times. Among other things, we talked about the town's need for a modern hospital. The Parkview Hospital is the result of his dreams and plans.

When I was trying to make up my mind whether or not I should return to private practice, it was Ron Bettie who gave me the final push and not only persuaded me to return but provided the office space while he was away in Africa.

Dr. Bettie possessed a quality of character that few people have; namely, he was **SOMEONE YOU COULD TALK TO**. I shall miss him.

I want to close by quoting an epitaph written for another physician which is an appropriate epitaph for Dr. Bettie.

"A man of great determination, though soft-spoken, imaginative and resourceful, with kindly eyes, one felt in his presence a vitality and keenness of perception . . . His kindness, warmth and modesty are legendary."

I mourn the death of Ron Bettie. I do not, however, mourn his death as much as I rejoice that he lived.

LOUIS BACHRACH, M.D.
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News, Notes and Announcements

Tentative Conference Schedule
Department of Surgery
Maine Medical Center, Portland, Maine

- 1975
*11/20 Nabseth
ORGAN TRANSPLANTATION, PRESERVA-
TION & BANKING
11/27 MORTALITY
12/ 4 Stocks
THYROID TUMORS
12/11 Collins, Britton
PORTAL HYPERTENSION AT MMC
*12/18 Deterline
1976
1/ 8 MORTALITY
1/15 Waterhouse, Ferris
AIR UNDER THE DIAPHRAGM
* 1/22 MacArthur
HEPATIC ABSCESS AND RESECTION
1/29 MORTALITY
2/ 5 Stocks
SOFT TISSUE TUMORS / Waterhouse, Dinan
ANEURYSMS AT MMC
2/12 SURGICAL CPC
* 2/19
2/26 MORTALITY
3/ 4 No Conference. Webber Dq, March 5, 6. George
Zuidema, Guest
3/11 Morton, Lutes, Hiebert, White
CORONARY ARTERY RESULTS MMC
* 3/18
3/25 MORTALITY
4/ 1 Anderson, Shapiro
RECTAL CANCER AT MMC
4/ 8 Barron, Pennoyer
RECURRENT HERNIAS
* 4/15
4/22 Bidwell
CEREBRAL ANEURYSM AT MMC /
MORTALITY
4/29 MacLaughlin, Britton
TRAUMA AT MMC
5/13 SURGICAL CPC
* 5/20
5/27 MORTALITY
6/ 3 Browne, Dillihunt, Sommers, Allen
LUMPS, BUMPS, RASHES, AND BOILS
6/10 Goldfarb
GRANULOMATOUS ENTERITIS
* 6/17
6/25 Waterhouse, Collins, Ferris
RESIDENTS REPORT
*Guest

Phenomenology and Treatment of Depression

presented by the Department of Psychiatry
Baylor College of Medicine, Houston
December 4-5, 1975

The Shamrock Hilton Hotel, Houston

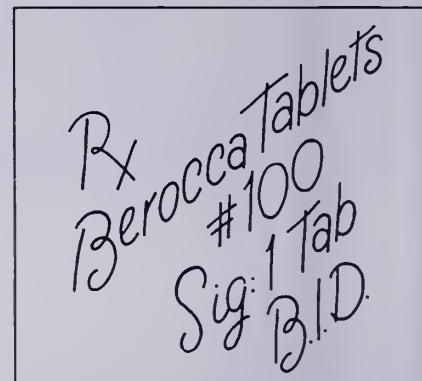
Depressive disorders constitute the most common type of psychopathology confronted by the psychiatrist, internist, and physician in family and general practice. Etiology, diagnosis, and treatment of depression, although still imperfectly understood,

Continued on Page 332

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Number 11

Emergency Medicine

W. P. CARTER, JR., M.D.* and FRANK H. LAWRENCE, M.D.**

HISTORICAL PERSPECTIVE

Emergency medical care in the United States has historically taken a back seat in the health care delivery system. In comparison with Russian Emergency Medical Services, the United States has lagged far behind in developing a comprehensive system for the treatment of the acutely ill.¹ In the Soviet Union, Emergency Medicine has held specialty status since 1919; such is not the case in the United States where Emergency Medical Services (EMS) has developed slowly until recent years. As a result of the burden placed upon the ambulatory care systems of hospitals across the country, emergency rooms have often functioned as a chaotic meeting place for emergent and non-emergent patients. To meet the patient demands, an estimated 15,000 physicians in the United States are now practicing in emergency rooms. Relatively few have specific emergency training, a high level of competence or experience in the management of emergencies. However, this situation is changing.

In 1968, the American College of Emergency Physicians (ACEP) was founded by eight physicians. Presently, with over 5,000 members, the ACEP ranks fifth in size among 125 national medical societies. In 1973, the American Medical Association approved Emergency Medicine in its 25th Scientific Session and in 1974, the American Medical Association House of Delegates approved the concept of residency programs in Emergency Medicine. The result has been an enthusiastic interest among medical school graduates in Emergency

Medicine as a career. Residency programs have been developed across the country with approximately 120 residents currently training for careers in Emergency Medicine.

THE EMERGENCY PHYSICIAN

Traditionally, the Emergency Room has provided a noisy, crowded, stressful environment, where, for 24 hours a day, 7 days a week, physicians worked frantically in an attempt to cope with a multitude of medical problems. The patients, rather than the administration, developed the system, demanding "to be seen" even if their illnesses were minor ones. The staffing physician, with perhaps a variable degree of knowledge and modicum of expertise in emergency principles (and sometimes a disinterest in what he was doing) practiced a combination of emergency medicine and general medicine. Staffing often has been via the ophthalmologist or psychiatrist who got "the duty" because it was "his turn," or via the moonlighting intern or resident seeking primarily financial gain while training in some other specialty. With earlier specialization in medical education, it has become seemingly unimportant to the specializing intern or resident to learn to manage the full range of medical and surgical problems. The lack of interest and training in a discipline felt to be unrelated to his intended specialty, discouraged the house officer from learning to effectively handle a wide variety of emergency medical problems.

Often considered trauma stations, emergency rooms have been felt to be the domain of the individual possessing a surgical expertise. However, a review of the annual visits to most emergency rooms dispels that notion. Less than 5% of the ad-

*Attending Physician, Emergency Division, Maine Medical Center, Portland, Maine 04102.

**Director, Emergency Division, Maine Medical Center, Portland, Maine 04102.

missions to the Maine Medical Center† represented acute-surgical emergencies in 1974.

Today, the emergency physician represents a new breed of doctor. He is not in an emergency room because he could not make it in another specialty or wishes to "retire," but because he finds emergency health care academically stimulating and intellectually satisfying. Practicing far more than glorified first aid, the emergency physician effectively utilizes a multitude of medical and surgical disciplines. From the convulsing child to the cardiac arrest, through the psychotic and the overdose, the properly trained emergency physician reacts with diagnostic and therapeutic decisiveness. The major factor which makes the emergency physician distinctive is his broad range of skills. If a trauma patient is brought into an emergency room setting, an orthopedic surgeon treats the broken bones, a chest surgeon treats the thoracic injury, a neurosurgeon treats the head injury and a general surgeon treats the ruptured intraabdominal viscus. The emergency physician must possess the ability to make rapid diagnoses and the skills to initiate appropriate treatment; secondarily, the emergency physician must communicate with and coordinate appropriate specialists. Because the emergency physician is faced with a wide variety of problems, his education is an unusual one in today's medical world when most areas of study lead "vertically" into a single area of study as opposed to "horizontally" through many areas of study. The educational objectives of emergency physicians are most closely akin to those of the family practitioners, but while the family practitioner can refer his patient to the specialist for further evaluation, the emergency physician must often act immediately if he is to intervene in a patient's impending demise.

Throughout the United States a group of first career emergency physicians is emerging. Their medical backgrounds are often diverse, but their goal is uniformly to participate in and deliver high quality emergency care; they are seeking and obtaining the type of education they need to attain their career objective.

EMERGENCY MEDICAL SERVICES

The transportation and pre-hospital treatment of the acutely ill or injured are vital elements which have been ignored in the past. With recognition of the fact that morbidity and mortality can be decreased with better pre-hospital care, emergency physicians have focused a great deal of attention on the patient prior to his arrival at the hospital.

In 1973, Congress enacted the Emergency Medical Systems Act which recognized the need for improvement in the present state of Emergency

†Maine Medical Center, Portland, Maine (Statistics — Emergency Division)

Medical Services. By attempting to upgrade the quality of pre-hospital transportation of the acutely injured, the goal of the act is to save lives; Boyd² has shown that a comprehensive treatment-transportation system can do just that. Historically, United States ambulances have been staffed by individuals on a volunteer basis. Like the doctor on duty in the emergency room the volunteers' knowledge and experience were less than optimal; levels of competency were infrequently evaluated and consequently not modified. For years the concept of putting the injured "in the back of the wagon" and "running" to the hospital was what any "good" ambulance driver did. Federal and public demand as well as the concern of the emergency physician have produced sweeping changes in emergency health care delivery. Courses in basic and advanced life support are now being offered to ambulance attendants. The Emergency Medical Technician (EMT) after 81 hours of instruction receives certification by national examination thereby insuring high standards of competence in the pre-hospital phase of patient care. In Maine, the Vocational Technical Institutes offer emergency medical technician education in conjunction with the Department of Health and Welfare. The student response and enthusiasm have been tremendous and the bulk of the teaching has been provided by the full-time emergency nurses and physicians. The EMT with education in basic life support is now staffing ambulances in many areas of the State.

In Portland, Maine, MEDCU (Medical Crisis Unit) an ambulance service staffed by salaried EMT's recently has come into existence through the support of federal monies. Like many of the volunteer services, MEDCU offers 24-hour a day service to the public and forms a prototype for pre-hospital transportation in the State's emergency medical system. At present there is no plan in Maine to provide pre-hospital emergency care in other areas by a similar system.

Maine's rural population and geography present difficulties shared by many states in offering adequate emergency medical service to the entire population. (In the Soviet Union, physicians go directly to the victim; there are over 650,000 physicians in Russia³ — more than in the United States, Great Britain, and France combined.) At present, some areas of the United States are utilizing physicians in ambulances but this alternative is not logistically feasible for the entire country. Thus, the well trained EMT has become and will remain a crucial element in pre-hospital emergency care.

Nurses, like physicians, have become interested in specializing in Emergency Medicine. Emergency Department nurses now have educational prerequisites and standards which are similar to those followed by nurses who staff coronary care and in-

tensive care units. At the Maine Medical Center Emergency Division, selected nurses participate in a 10-week course which prepares the nurse to perform brief histories and physical examinations and arrive at a tentative diagnosis. This additional education facilitates triage and consequently the skills possessed by an experienced nurse are more effectively utilized. Many nurses who staff emergency departments now belong to a specialized professional society, the Emergency Division Nurses Association (EDNA) which promotes education and meaningful dialogue between nurses and hospitals.

PUBLIC EDUCATION

Public education is fundamental in developing good emergency medical care. The emergency physician must not only be competent in providing good primary care but must also educate the public as to the function and proper utilization of an emergency facility. Statistics at the Maine Medical Center reveal that less than 3% of patients presenting to the Emergency Division are life-threatening emergencies. However, every patient presenting to an emergency unit considers his problem an urgent one, albeit for personal rather than medical reasons. While the unavailability of primary care physicians often forces patients into the emergency room for treatment, patient misconception and consequent misuse of emergency facilities is primarily a result of inadequate public education. The result — inundation of emergency rooms with inappropriate pa-

tients — has been high hospital costs and subsequent high charges to the non-emergency patient. Elaborate systems of triage have been developed out of necessity to insure that true emergencies receive prompt recognition and attention.⁴

SUMMARY

The public demands and deserves high quality emergency care. In the United States, the team approach to emergency medical care, with Emergency Medical Technicians performing pre-hospital treatment and hospital-based physicians and nurses performing definitive care, is providing the basis for improved emergency medical services. Communities, organizations, and hospitals have recognized the necessity for well-trained personnel. The progress made in improved staffing of emergency facilities throughout Maine in the last five years is evident and with improved pre-hospital care and full-time emergency physicians, the Emergency Medical System is establishing a noteworthy position in the sphere of health care delivery. Emergency Medicine, as a developing specialty, is meeting the challenge produced by the acutely ill.

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Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The bylaws of the Maine Medical Association were amended in June of 1973 as follows: Chapter I, Section 11, — "Each member of the Maine Medical Association shall be required to report his activities in continuing medical education every year according to a format provided by the Committee on Continuing Medical Education."

Only active, dues-paying members are required to report this year.

Please fill in your activity report promptly and return to the M.M.A. office, P.O. Box 250, Brunswick, Maine 04011.

Health Care Delivery in Maine III: Evaluating the Level of Hospital Performance

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Hospitalizations for common surgical and medical conditions vary extensively among different planning regions and Hospital Service Areas in the State of Maine.^{1,2} We have suggested these differences should be taken into account in reaching planning or regulatory decisions and in selecting problems for peer review. However, to be taken into account, they must be measured directly or by surrogate indicators. Traditionally, the measures of use of health care by the population-at-risk have not been available for regional planning and regulation or for decision making by hospital administrators and physician staffs. The indicators of performance that are generally available provide comparisons among individual hospitals in their intensity of care per case treated, their need for facilities and the efficiency of management but not of their individual or collective impact on populations living in neighboring communities.

The purpose of this article is to test the utility of institutional indicators in predicting variations in per capita expenditures and bed-use rate. We are interested in the relative importance of intensity of care measures, length of stay, cost per case and cost per day in hospital, and the incidence of hospitalization in determining resource use. Studies are made of admissions for specific diagnoses and procedures and of hospitalizations for all causes. We examine the value of the occupancy rate and bed turnover rate in predicting per capita expenditures and the availability and use of beds.

Our studies show that institutional indicators are poor predictors of population rate of use and that a direct, epidemiologic approach to evaluation of performance is necessary if basic issues concerning medical necessity and distributional equity are to be identified. Case studies of selected hospital service areas in Maine and Vermont are presented to illustrate that planning, management or regulatory de-

cisions which rely solely on institutional indicators are in hazard of increasing inequalities in distribution of resources among neighboring communities which show no evidence of differences in need for service. On the other hand, population-based data can aid decision makers in distinguishing inappropriate use of hospitals from shortage of bed supply.

METHODS

The measurement of per capita use of hospital services by residents of hospital service areas (HSAs) or planning regions has been described in previous articles.^{1,2} Data on incidence and resource use for individual procedures and for the condition causing admission to hospitals are for Maine hospital service areas, 1973. The medical conditions studied in this paper are acute and chronic infections of the respiratory tract; the International Classification of Diseases used in these diagnostic groupings have been previously given.² Per capita hospital bed use is measured by the patient day rate which is the number of days residents of an HSA spend in hospitals per 1,000 residents. In determining the rate, all hospital days are counted, whether the hospitalization is at a local or out-of-area facility. Incidence rates likewise reflect total population use. Since all Maine and Vermont short-term hospitals contribute data to the study, our statistics include nearly all uses of hospitalizations by residents of these areas.

For specific medical conditions and surgical procedures, the importance of average length of stay and incidence in predicting bed use is studied across the 13 largest Maine HSAs. All the HSAs have populations greater than 20,000 persons. Area-wide average length of stay is obtained by dividing the number of resident patient days by the number of resident discharges from hospital, without regard to location of hospital. Average charge per case is reported only by hospitals participating in the Maine Data Service Program and is therefore not available for all Maine hospitals. For the 8 HSAs with populations ranging from 20 to 50 thousand persons, data are available for each local hospital, and in these areas we use charges as our estimator of cost per case and per capita cost per procedure. For tonsillectomy, hysterectomy, her-

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niorrhaphy, hemorrhoidectomy and cholecystectomy, charges per case data is available. Within each area, the majority of these procedures is performed at local hospitals. For a given procedure, total area charges are estimated by multiplying for each local hospital the number of procedures performed on area residents by the hospital specific average charge per case and summing across the experience of all hospitals performing the procedure on area residents. Out-of-area hospital use included some hospitals not reporting average charge per case and these are estimated by the State average of all reporting hospitals.

The relationship of institutional indicators and hospital discharge rate to per capita expenditure and bed use for all hospitalizations is studied using data from 13 Vermont and 28 Maine HSAs. The smallest Maine HSA has 10,000 residents; the smallest Vermont HSA, 8,000. Vermont data are for 1969; Maine data are for 1971, and patient day data are not available for this year.[†] In areas with more than one local hospital, institutional indicators are a weighted average of the experience of each local hospital. Percent of occupancy is obtained by dividing the average daily census by the number of available beds. The bed turnover rate is defined as average number of patients treated per bed per year. Average cost per day in hospital was obtained from Blue Cross and is available for Vermont only.

Estimates for total per capita hospital expenditures in an area are obtained by allocation of annual total expenditure of each individual hospital to the HSA of residence of its patients. For example, if 10 percent of the patients admitted to a given hospital live in a particular HSA, 10 percent of the hospital's annual expenditures are assigned to that area. The sum of all hospitals' contributions to the service area provides a measure of total expenditure. An estimate of per capita availability of beds is obtained by allocating the bed supply of each hospital to the area of origin of its patients, using the same estimating procedure as for per capita expenditures. Data on planning decisions in Vermont are from published reports or from planning documents available to the authors.

The principal statistical issue is the correspondence between two ways of viewing hospital performance: from the perspective of the institutions and from the perspective of the populations who are served by the institutions. We are interested in learning the extent of the association of institutional performance indicators with the population's availability and use of beds or expenditures.

[†]Maine data for this part of the study were obtained during a feasibility study of developing a population-based data system for Maine.

We also want to know the extent to which variation in use of dollars and beds relate to variations in incidence of hospitalization. The statistic we use to characterize the correspondence among indicators is the "explained variance" or " R^2 " statistic which is square of the correlation coefficient. The correlation coefficient itself ranges from -1.0 to +1.0; the stronger the relationship the nearer the value of the coefficient is to 1.0; weak relationships are near zero. The sign of the coefficient indicates the direction of association (a negative sign means the value of one indicator increases as the other decreases). The squared correlation coefficient is usually expressed as a percent and represents an estimate of the variance or difference among the values of one variable which is explained by difference among the value of a second.

RESULTS

Determinants of Per Capita Expenditures and Bed Use

The mean, range and coefficient of variation of all variables and the correlation coefficients between relevant variables are given in the Appendix.

For specific medical and surgical conditions. Average length of hospital stay and cost per case are not important predictors of per capita use of beds or charges for common surgical conditions and for respiratory disease illnesses (Figures 1 and 2). In only one of the ten cases do they explain a majority of the variation is per capita consumption. In contrast, there are strong linear associations between bed use and per capita charges and the incidence rate of hospitalizations for specific conditions and procedures. Although the variation in length of stay and average charge per case for specific procedures and conditions is substantial, these measures show little correlation with incidence rate (Appendix Tables). Incidence rates of hospitalization show greater variation than length of stay and are the immediate determinant of variation in bed use and per capita charges.

For all hospitalizations. For all causes, the relationship between incidence and bed use and expenditures is considerably weaker than for specific conditions or procedures (Table 1). Among the 28 Maine Hospital Service Areas, the incidence rate accounts for about 34 percent of the variation in estimated expenditures. In Vermont, incidence rate has little value in predicting per capita expenditures or bed use. The weakening of the relationship between incidence and resource use reflects the difference in mix of procedures and conditions treated in hospitals in the neighboring areas. Variation in average length of stay also counts for little of the variation in per capita expenditures. The strongest relationship is between per capita expenditures and average charges per day in hospital. However,

FIGURE 1

CONTRIBUTION OF AREA-WIDE AVERAGE LENGTH OF STAY AND INCIDENCE OF HOSPITALIZATION TO PER CAPITA USE OF HOSPITAL BEDS FOR COMMON SURGICAL PROCEDURES AND RESPIRATORY DISEASES. THIRTEEN LARGEST MAINE HOSPITAL SERVICE AREAS, 1973.

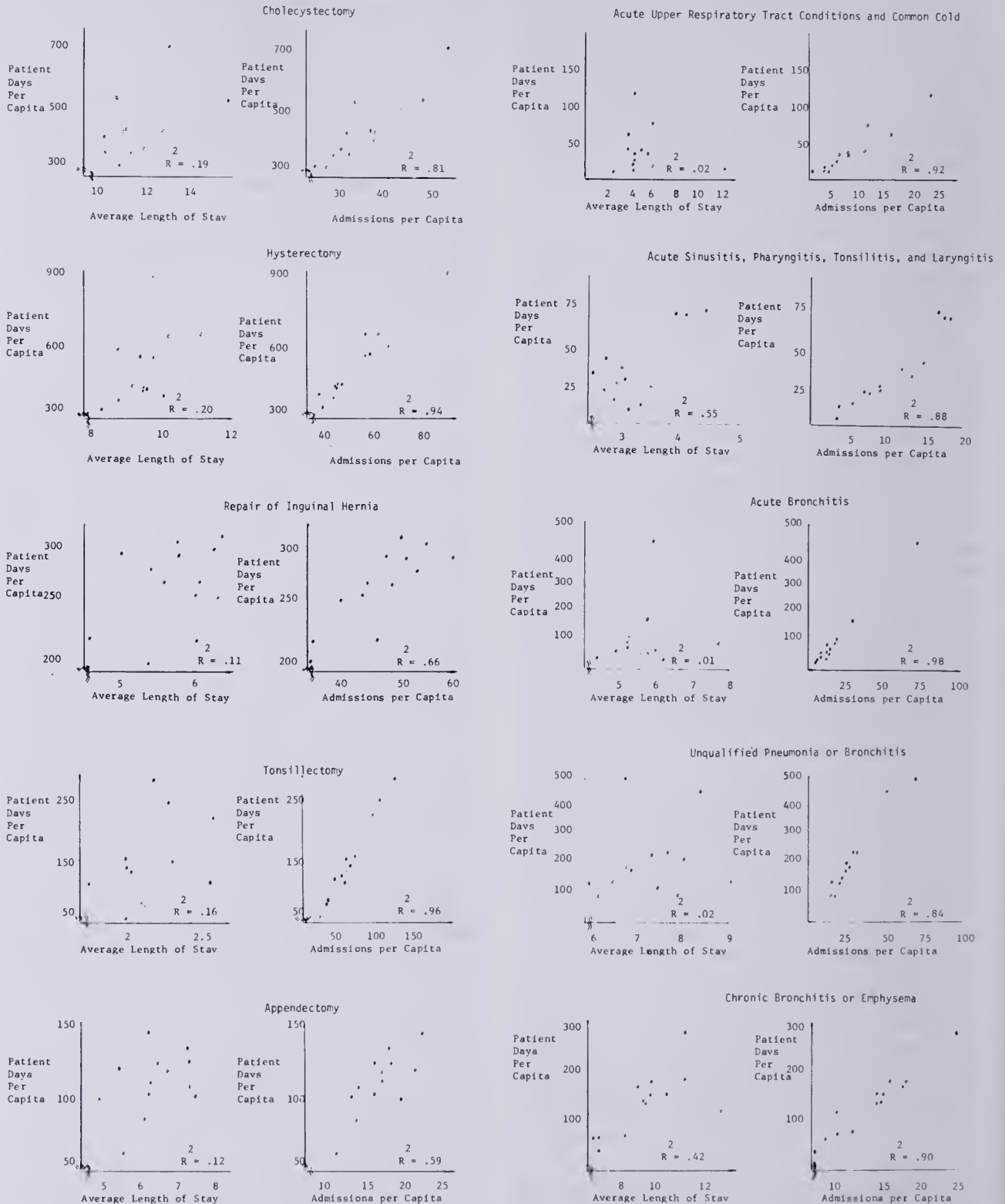
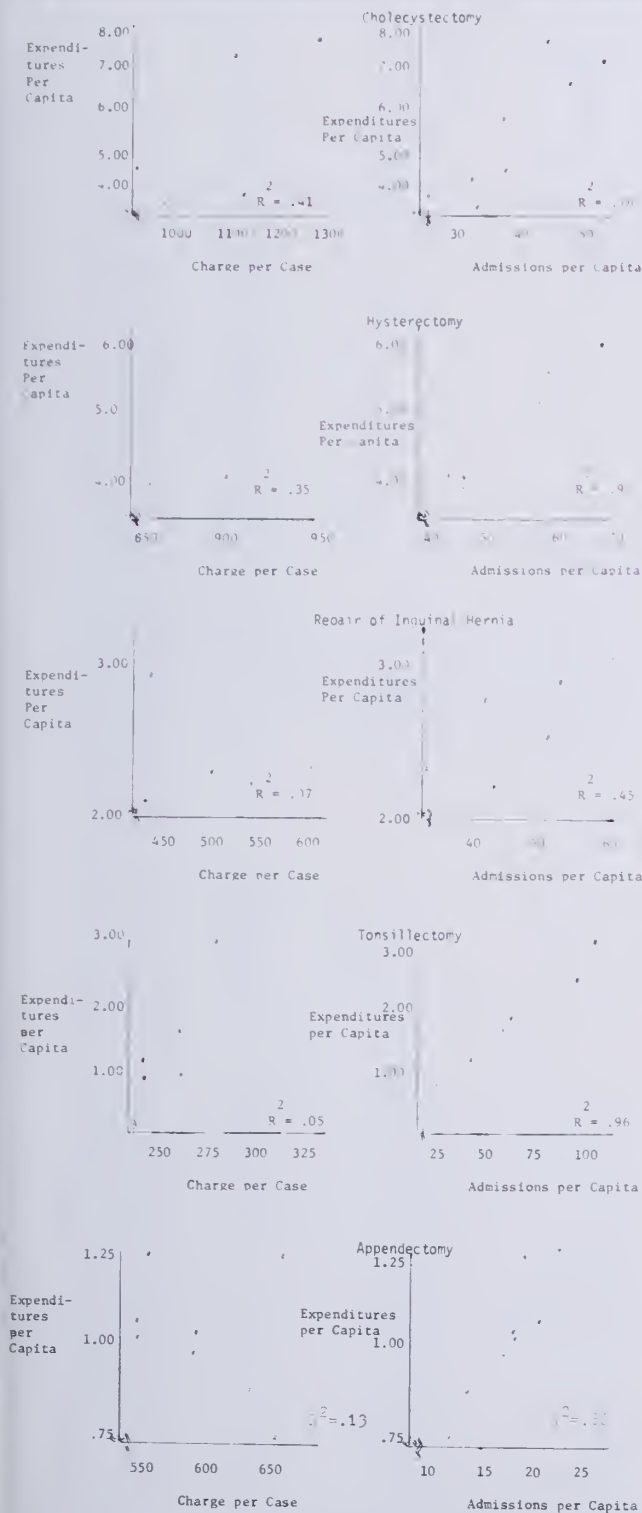


FIGURE 2

CONTRIBUTION OF AREA-WIDE CHARGE PER CASE AND INCIDENCE OF HOSPITALIZATION TO ESTIMATED PER CAPITA EXPENDITURES FOR COMMON SURGICAL PROCEDURES. EIGHT MAINE HOSPITAL SERVICE AREAS, 1973.



the differences in per capita expenditures which are "explained" by this variable are less than 40 percent and the indicator, taken alone, is an insufficient measure of population expenditure.

Performance Evaluation and Institutional Indicators

Table 1 shows that differences in bed turnover rates as well as length of stay and cost per day in hospital are unreliable indicators of relative per capita expenditures. It also shows that variation in percent of occupancy among areas has little correspondence with per capita expenditures, or availability and use of hospital beds. These statistical issues are illustrated in the following case studies.

A profile of hospital performance in five Maine areas. Table 2 shows the per capita incidence of hospitalization, expenditures and bed availability and use, and the status of three institutional indicators which are considered to be indicative of the efficiency of hospital performance and the need for beds. Although the institutional indicator of bed availability, (percent of occupancy) is nearly identical in four of the five areas, the patient day rate which describes bed use by the population varies from 800 to 1,625 days per 1000 persons per year. The area with the highest bed turnover rate (Area IV) has the highest rate of hospitalization, the most patient days and expenditures per capita, and has the most available beds. Previously we have found that this area, compared to the other four, has a high rate of common surgical procedures, particularly tonsillectomy and hemorrhoidectomy.¹ Area IV's length of stay is nearly the same as Area V which has the lowest incidence rate and per capita expenditures of the five areas. It is apparent that the large differences in resource use among areas are not indicated by conventional institution-based indicators.

Public Planning and Regulation in Vermont Hospital Service Areas

Planners and regulators depend on institutional indicators in reaching decisions on the allocation of resources and in regulating the price of health care. Because of the low correspondence between institutional indicators and the underlying consumptive patterns of the populations, the impact of public decisions on the equality of resource distribution among neighboring hospital service areas is usually unknown. In Vermont, where population-based data have been available since 1969, case studies can be made of public decisions made during that period from the perspective of the population they affect. Table 3 presents data on the number of hospitals in each area, the incidence of hospitalization, per capita expenditures and bed use and features of public decisions affecting three Vermont Hospital

APPENDIX TABLE 1

MEAN, RANGE, AND COEFFICIENT OF VARIATION. INSTITUTIONAL AND PER CAPITA INDICATORS OF HOSPITAL PERFORMANCES
IN SELECTED MAINE AND VERMONT HOSPITAL SERVICE AREAS.

	<i>Lowest Value</i>	<i>Highest Value</i>	<i>Mean</i>	<i>Coefficient of Variation</i>
Specific Medical and Surgical Causes of Admission				
Cholecystectomy				
Area-wide Length of Stay	10.22	15.26	11.51	0.12
Patient Days per 10,000	293	700	420	0.27
Admissions per 10,000	25	55	36	0.24
Charges per case (\$)*	910	1297	1083	0.11
Charges per capita (\$)*	3.58	7.94	5.52	0.31
Hysterectomy				
Area-wide Length of Stay	8.28	10.95	9.43	0.07
Patient Days per 10,000	347	882	521	0.28
Admissions per 10,000	40	92	55	0.26
Charges per case (\$)*	842	947	895	0.04
Charges per capita (\$)*	3.61	6.16	4.63	0.21
Repair of Inguinal Hernia				
Area-wide Length of Stay	4.58	6.35	5.74	0.09
Patient Days per 10,000	182	312	261	0.16
Admissions per 10,000	34	58	46	0.16
Charges per case (\$)*	432	609	525	0.11
Charges per capita (\$)*	2.14	3.27	2.66	0.15
Tonsillectomy				
Area-wide Length of Stay	1.77	2.60	2.20	0.10
Patient Days per 10,000	50	279	140	0.49
Admissions per 10,000	24	126	64	0.47
Charges per case (\$)*	242	304	268	0.08
Charges per capita (\$)*	0.74	3.00	1.51	0.53
Appendectomy				
Area-wide Length of Stay	4.92	7.51	6.44	0.13
Patient Days per 10,000	64	145	110	0.19
Admissions per 10,000	11	23	17	0.20
Charges per case (\$)*	542	657	594	0.08
Charges per capita (\$)*	0.74	1.22	1.02	0.16
Acute Upper Respiratory Tract Condition and Common Cold				
Area-wide Length of Stay	2.54	12.50	5.15	0.47
Patient Days per 10,000	11	115	38	0.79
Admissions per 10,000	0.9	25	8	0.79
Acute Sinusitis, Pharyngitis, Tonsillitis, and Laryngitis				
Area-wide Length of Stay	2.51	4.49	3.28	0.18
Patient Days per 10,000	11	77	37	0.64
Admissions per 10,000	3	19	11	0.50
Acute Bronchitis				
Area-wide Length of Stay	4.50	7.79	5.76	0.13
Patient Days per 10,000	31	427	102	1.02
Admissions per 10,000	5	72	18	0.99
Unqualified Pneumonia or Bronchitis				
Area-wide Length of Stay	6.05	8.92	7.29	0.12
Patient Days per 10,000	85	482	204	0.60
Admissions per 10,000	15	71	28	0.57
Chronic Bronchitis or Emphysema				
Area-wide Length of Stay	6.89	12.72	9.29	0.18
Patient Days per 10,000	41	281	138	0.45
Admissions per 10,000	6	26	14	0.36
1971 Maine Data Hospital Expenditures per capita (\$)				
Admissions per 1,000	33	121	79	0.24
Percent Occupancy (Local Hospital)	119	227	168	0.20
Average Length of Stay (Local Hospital)	49	93	69	0.13
Bed Turnover Rate (Local Hospital)	4.3	8.7	6.8	0.16
1969 Vermont Data Hospital Expenditures per capita (\$)				
Admissions per 1,000	28	60	38	0.21
Percent Occupancy (Local Hospital)	58	120	82	0.19
Average Length of Stay (Local Hospital)	115	196	143	0.17
Bed Turnover Rate (Local Hospital)	63	100	81	0.13
Average Cost per Day (Local Hospital) (\$)	5.6	9.5	7.5	0.16
Bed Use (Total Patient days per 1,000)	31	47	40	0.13
	32	41	36	0.14
	897	1578	1221	0.14

*for 8 Maine Hospital Service Areas included in Cost Study, 1973

APPENDIX TABLE 2

CORRELATION MATRIX: PATIENT DAY RATE, AREA-WIDE AVERAGE LENGTH OF STAY AND ADMISSION RATE FOR COMMON MEDICAL AND SURGICAL HOSPITALIZATIONS, 13 MAINE HOSPITAL SERVICE AREAS, 1973.
(Pearson Correlation Coefficients)

KEY	
1	= Patient Days per 10,000
2	= Area-wide Average Length of Stay
3	= Admissions per 10,000

Cholecystectomy

	(2)	(3)
(1)	0.44	0.90
	(2)	0.03

Hysterectomy

	(2)	(3)
(1)	0.45	0.97
	(2)	0.22

Repair of Inguinal Hernia

	(2)	(3)
(1)	0.33	0.81
	(2)	-0.26

Tonsillectomy

	(2)	(3)
(1)	0.40	0.98
	(2)	0.28

Acute Upper Respiratory Tract Condition and Common Cold

	(2)	(3)
(1)	-0.15	0.96
	(2)	-0.31

Acute Sinusitis, Pharyngitis, Tonsillitis and Laryngitis

	(2)	(3)
(1)	0.74	0.94
	(2)	0.49

Appendectomy

	(2)	(3)
(1)	0.34	0.77
	(2)	-0.31

Unqualified Pneumonia or Bronchitis

	(2)	(3)
(1)	0.13	0.97
	(2)	<-0.01

Chronic Bronchitis or Emphysema

	(2)	(3)
(1)	0.65	0.95
	(2)	0.43

Acute Bronchitis

	(2)	(3)
(1)	0.11	0.99
	(2)	0.02

APPENDIX TABLE 3

CORRELATION MATRIX: ESTIMATED EXPENDITURES PER CAPITA, AREA-WIDE AVERAGE CHARGE PER CASE AND ADMISSION RATE FOR FIVE COMMON SURGICAL PROCEDURES, 8 MAINE HOSPITAL SERVICE AREAS, 1973.
(Pearson Correlation Coefficients)

KEY	
1	= Charges Per Capita (Estimated Expenditures)
2	= Area-wide Average Charge per Case
3	= Admissions per 10,000

Cholecystectomy

	(2)	(3)
(1)	0.64	0.87
	(2)	0.23

Hysterectomy

	(2)	(3)
(1)	0.59	0.98
	(2)	0.44

Repair of Inguinal Hernia

	(2)	(3)
(1)	0.26	0.67
	(2)	-0.51

Tonsillectomy

	(2)	(3)
(1)	0.23	0.98
	(2)	0.14

Appendectomy

	(2)	(3)
(1)	-0.36	0.93
	(2)	-0.66

Service Areas in the years 1969 through 1973. Residents living in these three areas have similar insurance coverage, illness rates, physician availability and behavior in seeking physician care.³ Among the three areas, the volume of hospitalized services received varies considerably; there is a two-fold difference in per capita expenditures for hospitals and rate of surgery; bed availability varies from 3.4 to 5.9.

Price setting. During Phase II of the Economic Stabilization Act, the hospitals located in Area II and Area III requested exceptions to the imposed 5 percent limit on annual increases in price of a day in hospital. The hospital located in Area III retired

its application prior to public hearing; Area III ranked 12th among the 13 areas in annual per capita expenditures for hospital. Area II's hospital received authorization for an increase in price in excess of 5%; the area ranked second in 1969 in per capita expenditures.⁴

Insurance regulation. The per capita reimbursements under Medicare Part B in the three areas are shown in Table 3. Reimbursements per enrolled individual in Medicare Program for 1972 ranged from an estimated low of 92 to a high of 162 dollars per enrollee among the three areas.⁴ Table 3 also estimates the flow of dollars in or out of these areas which are a consequence of Federal policies in

APPENDIX TABLE 4

CORRELATION MATRIX: PARAMETERS OF HOSPITAL UTILIZATION, 28 MAINE HOSPITAL SERVICE AREAS, 1971.
(Pearson Correlation Coefficients)

	(1)	(2)	(3)	(4)	(5)
Hospital Expenditures Per Capita (\$)	(1)	.59	.13	.22	-.11
Admissions per 1,000		(2)	-.04	-.21	.17
Percent Occupancy (local hospital)			(3)	.16	.42
Average Length of Stay (local hospital)				(4)	-.76
Bed Turnover Rate (local hospital)					(5)

APPENDIX TABLE 5

CORRELATION MATRIX: PARAMETERS OF HOSPITAL UTILIZATION, 13 VERMONT HOSPITAL SERVICE AREAS, 1969.
(Pearson Correlation Coefficients)

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Hospital Expenditures per capita (\$)		.21	-.07	.46	-.58	.68	.47
Admissions per 1,000			-.17	-.37	.32	-.43	.73
Percent Occupancy (local hospital)				.57	.28	.00	.24
Average Length of Stay (local hospital)					-.62	.48	.22
Bed Turnover Rate (local hospital)						-.59	.02
Average Cost per Day (local hospital) (\$)							-.15
Bed Use (Total Patient Days per 1,000)							

determining price of premiums for the program. The funds for Medicare Part B are from a 50% contribution from the enrollee and a 50% contribution from the Federal treasury, based on the *national* average per capita rate of reimbursement. However, because medical resources are used differently there are subsidizations (income transfers) among areas. In 1972, the National average reimbursement under Medicare Part B was about 139 dollars per enrollee. Enrollees living in Area I enjoyed a subsidy of 23 dollars per enrollee while enrollees in Area III contributed 47 dollars per capita towards the subsidization of enrollees living in high expenditures areas.[†]

Assessing need for hospital beds. Two of the three areas share a common border with Hill-Burton planning areas and it is possible to relate the Hill-Burton's agency's assessment of need for additional facilities with concurrent consumption rates.⁴ In 1969, the Hill-Burton Agency determined that the hospital located in the area of high utilization (Area II) needed a 44 percent increase in bed supply. (Compared to all Vermont areas, Area II ranged second in incidence of hospitalization and first in use of surgery in 1969). In contrast, the area ranking lowest among the thirteen areas in use of surgery, incidence of hospitalization and bed use was assigned a low (2%) need for additional resources. Hill-Burton determinations were based on percentage of occupancy indicators.

Surgical facilities. The Vermont State Comprehensive Health Planning Agency was asked to review an application for building additional surgical

TABLE 1

PERCENT OF VARIANCE IN PER CAPITA BED USE AND EXPENDITURES ASSOCIATED WITH VARIANCE IN INCIDENCE OF HOSPITALIZATION AND OF INDICATORS OF INSTITUTIONAL PERFORMANCE FOR ALL CAUSES OF ADMISSION. 13 VERMONT (1969) AND 28 MAINE (1971), HOSPITAL SERVICE AREAS.

	Per capita expenditures Maine	Bed Use Vermont	Bed Use Vermont
Average length of stay in local hospital(s)	4	21	5
Average cost per day of care in local hospital(s)	NA	38	5
Percent of occupancy in local hospital(s)	1	<1	5
Bed turnover rate in local hospital(s)	1	33	<1
Per capita incidence rate in area for all hospitalization	34	5	21

facilities at one of two hospitals located in Area 1. Although the area ranked third from highest among the 13 areas in overall surgery rates and highest in per capita expenditures, institutional needs and indicators were the criteria for the decision which resulted in the construction of the proposed surgical facilities.⁵

Coronary care beds. Table 4 shows the status of investment in coronary care units (CCUs) in ten Vermont HSAs in 1971. The areas are ranked on per capita expenditures. During 1971, clinical management of coronary care was regionalized through a management committee established under Regional Medical Program auspices. The committee was responsible for establishing and publishing guidelines for the treatment of patients in the CCU of each of the region's hospitals. It was also responsible for making recommendations on the necessity of further capital investment in coronary

[†]This estimate assumes an average contribution to the Federal Treasury in each area.

TABLE 2

PROFILE OF INDICATORS OF PERFORMANCE IN FIVE LARGEST MAINE HOSPITAL SERVICE AREAS,
SHOWING INCIDENCE OF HOSPITALIZATION, PER CAPITA EXPENDITURES, PER CAPITA USE AND
AVAILABILITY OF BEDS AND THE STATUS OF THREE INSTITUTIONAL INDICATORS

	Incidence of hospitalization ^a	Patient days of care ^a	Available beds ^a	Per capita expenditures	INSTITUTIONAL INDICATORS		
					Percent of occupancy ^a	Average length stay ^a	Bed turnover rate ^a
Area I	145	1,104	4.1	102	73	7.6	33
Area II	153	1,244	5.0	92	73	8.1	31
Area III	157	1,054	4.2	75	65	6.7	34
Area IV	235	1,625	5.7	109	72	7.0	39
Area V	127	831	3.8	72	72	6.9	32

^aFor 1973 population rate per 1,000 population; incidence rate is age-adjusted

^a For 1971

TABLE 3

PROFILE OF POPULATION INDICATORS OF PERFORMANCE AND STATUS OF PLANNING OR REGULATORY DECISIONS IN THREE VERMONT HOSPITAL SERVICE AREAS (1969-1972)

	Area I	Area II	Area III
Number of local hospitals	2	1	1
Incidence of hospitalization			
All cases	145	195	122
Surgical cases	58	69	36
Hospital per capita expenditures	120	92	63
Reimbursement per enrollee,			
Medicare Part B	\$162	\$141	\$92
Bed availability	4.5	5.9	3.4
Planning or regulatory decisions			
Hill-Burton ascertainment of need (1969, percent increase in beds "needed")	NA	44%	2%
Surgical facilities built	Yes	NR	NR
Price commission exception to 5% limit on price	NR	Yes	No
Net flow of Medicare dollars in or out of area	-\$23	-\$2	-\$47

care units and for providing population-related data on each CCU admission. In 1971, the local hospital in Area I wished to increase the bed size of its CCU. The performance characteristics listed in Table 4 were reviewed by the management committee; based on its relative per capita ranking in utilization, resource use, bed availability, and the committee's knowledge of practice patterns at the hospital, the committee recommended against expansion of facilities and proposed, instead, further educational efforts to improve screening of patients prior to hospitalization.

DISCUSSION

Length of stay and cost per case are indicators of the intensity of care delivered to hospitalized patients. Together with the incidence rate, they determine the per capita expenditure or days in the hospital allocated to a population:

Expenditure per capita = admissions per capita
x average cost per case

Patient days per capita = admissions per capita
x average length of stay

TABLE 4

PER CAPITA USE OF CORONARY CARE UNIT (CCU) RESOURCES IN TEN VERMONT HOSPITAL SERVICE AREAS PARTICIPATING IN A REGIONAL MANAGEMENT PROGRAM FOR CORONARY ARTERY DISEASE
(Rates per 10,000 population, 40 years of age and older, 1969-70)

Area*	Available CCU Beds	Coronary Care Unit Nurses	Per Capita Expenditures
1	5.0	10.3	\$12.58
2	2.6	5.4	6.72
3	2.6	6.4	4.78
4	2.6	6.3	4.71
5	2.4	4.2	4.60
6	2.1	4.6	5.27
7	1.9	3.4	4.89
8	1.8	3.6	4.49
9	1.7	4.1	3.80
10	1.7	4.0	2.20

*Area ranked on CCU bed availability

For the common medical conditions and procedures studied above, the variation in length of stay and cost per case (which we have estimated by charges per case) is less than the variation in the incidence rate, and differences in the measures of intensity do not correlate with the incidence rate. Therefore, the incidence rate is much more important than intensity factors in determining expenditure and patient days for common surgical procedures. We can conclude that for the conditions we have studied in this paper the resource implications of differences in management within hospitals are less important than decisions to manage patients at the ambulatory or the institutional level of care.†

In our studies of use of hospital for all conditions, variations in admission rate, length of stay or cost per day in hospital each contribute little to variations in per capita expenditures or use of hospitals. The aggregate statistics describing hospital experience of an area — overall length of stay, admis-

†At the aggregate level of use of institutional care, there is little evidence of a substitution effect between hospital and nursing home placements. In 1969, among the 13 Vermont areas, the correlation coefficient for per capita expenditures for hospitals and for nursing homes is -.11; for admissions, it is .05.

sion and cost per case — are weighted averages of the different kinds of cases admitted to the hospital and reveal little information on the effect of hospitals on the populations they serve. There is also a poor correspondence between institutional indicators of hospital efficiency and overall per capita expenditures and bed use. Variations in bed turnover rates (which have been shown to be associated with cost per case)⁶ do not account for more than 33% of the variance in per capita expenditures. Among the five largest Maine Hospital Service Areas, the value indicating the most efficient use of hospitals was for hospitals serving the area with high admission, high tonsillectomy, high expenditure and high per capita available beds. Percent of occupancy, often viewed as an indicator of need for more beds, does not predict patient day rate or bed availability when viewed from the perspective of the population-at-risk. It is clear that this indicator — like all the institutional indicators we have studied — should be interpreted in conjunction with population based indicators.

Our review of planning and regulatory decisions in Vermont has shown that public decisions undertaken without benefit of population-based performance data can increase inequalities in distribution of resources among neighboring areas and establish income transfers through insurance mechanisms. However, when used within the context of a regionalized process for allocating capital for facility construction, experience in Vermont suggests that population-based data can help distinguish between "need" based on overutilization and need as defined by a consensus of regional experts. The key role of a regional management committee comprised principally of physicians in making the determination of need emphasizes the importance of including a properly constituted panel of physicians in the decision process established under certification of need programs.

CONCLUSIONS AND RECOMMENDATIONS

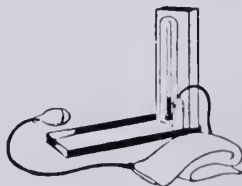
We have shown that institutional measures of the intensity of care, efficiency of operations or need for additional facilities do not predict per capita expenditures or the per capita use and availability of beds. Public decisions undertaken without benefit of population-based indicators have increased the inequality in distribution of resources among neighboring areas, and established income transfers through insurance mechanisms. Effective documentation of hospital performance requires an epidemiologic approach to the measurement problem. We recommend that such an approach be adopted in Maine where an existing data system can be adopted for use by PSRO, the State Certificate of Need program and by the new Health System Agency.

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Four Years Experience With Laparoscopy and Its Complications at the Maine Medical Center

WINTHROP S. MACLAUGHLIN, JR., M.D.* and ROGER RITTMASER**

INTRODUCTION

The laparoscope is a diagnostic and operative tool providing a low-risk, invasive technique for viewing the abdominal viscera. After discussing the history, technique, and complications of the procedure, this paper will review 435 laparoscopies performed at the Maine Medical Center between November 1971 and June 1974.

Laparoscopy was first introduced in Germany in 1901 using dogs as subjects. By 1913, the technique had achieved widespread diagnostic use by physicians throughout Europe. During the next fifty years, the laparoscope was employed sporadically in the United States, chiefly by gastroenterologists. Technical difficulties and a lack of familiarity with the procedure limited its acceptance. In 1944, the culdoscope was introduced to American gynecology, and for years it was used for many of the same indications as the laparoscope. More recently, improved fiberoptic lighting and sophisticated modern instrumentation has given the laparoscope more versatility than the traditional culdoscope. During the past five years papers by Fear,¹⁰ Cohen,^{7,8} and others^{11,16} have publicized the technique, demonstrating its efficacy in reducing cost and morbidity, and paving the way for its current popularity among gynecologists.

TECHNIQUE

The following technique describes the procedure as used during gynecologic operations. After appropriate preoperative evaluation and preparation for surgery, the patient is anesthetized with a non-explosive agent, employing both endotracheal intubation and skeletal muscle relaxants. The patient is then moved into the dorsal lithotomy position, and both the abdomen and perineum are prepped and draped. The bladder is then catheterized, and a pelvic exam is performed. A dilatation and curettage of the uterus is done when indicated. A vacuum-attached cannula or an analogous device is then inserted into the uterus to allow for easy manipulation of the uterus during laparoscopy.

The patient is then placed in a thirty degree Trendelenberg position and a pneumoperitoneum is created by first making a three millimeter transverse incision inferior to the lower border of the umbilicus. A Verres needle, connected to a CO₂ supply, is inserted through the incision into the abdominal cavity. The CO₂ is then introduced at a pressure which should not exceed 20 mmHg. A total of 2.5 to 5 liters of CO₂ (usually 3 liters suffices) is insufflated, depending on the size of the patient.

The Verres needle is removed, the incision widened slightly, and the laparoscope trocar passed through the skin and subcutaneous fascia. In a Z-tract¹³ fashion the trocar is moved along the surface of the peritoneum and then into the abdominal cavity at a 45-60 degree angle to the skin. The tip of the laparoscope is then pre-warmed in saline to the skin. The tip of the laparoscope is then pre-warmed in saline to prevent fogging. (If fogging occurs inside abdomen, the tip can be wiped against the uterine fundus to clear it¹³). Next the tip of the trocar is removed and the laparoscope inserted through the trocar sleeve. The fiberoptic cable from the light source is attached to the scope and the gas tubing is connected to the inlet valve.

For operative procedures and for manipulation of the abdominal organs, a second incision must be made for passage of the operative instrument. Using the laparoscope to transilluminate the abdominal wall, potential bleeding vessels are identified. The incision may be made hypochondrally, in either lower quadrant, or suprapubically. The last position is the most frequently used for tubal ligations and presents the least chance of penetrating a vessel in the abdominal wall.

Laparoscopic tubal cauterization has many variations, but most procedures follow the technique described by Steptoe.¹⁷ After insertion of the laparoscope, a second incision is made in the midline about halfway between the symphysis pubis and the umbilicus. The trocar and 6 millimeter cannula of the Palmer biopsy drill forceps is placed through the incision into the abdomen. Next the biopsy forceps replaces the trocar. The isthmus of one tube is grasped with the forceps about one centimeter from the cornu, and the forceps closed. After elevation of the tube, the coagulation current is

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passed until the tube and mesosalpinx blanch on either side of the forceps. The forceps are then moved about $\frac{3}{4}$ centimeter laterally along the tube and the procedure repeated. Inspection of the tube at this point should reveal about a two centimeter length of coagulation. The tube is cut with the forceps drill at the center of the coagulated area. After coagulating and severing both tubes, the forceps are removed and the incision closed.

Upon termination of laparoscopy, the laparoscope is removed, leaving the sheath in place. The abdominal gas is then allowed to escape with gentle pressure being placed on the abdominal wall. The sheath is removed, the abdomen checked for herniations, and the skin incision closed with clips or sutures. Anesthesia is then terminated.

COMPLICATIONS OF LAPAROSCOPY REPORTED IN THE LITERATURE

Complications of laparoscopy include those due to anesthesia, creation of the pneumoperitoneum, introduction of the trocar and sleeve, introduction and use of the laparoscope, and ancillary techniques employed with laparoscopy. The complications due to anesthesia are those complications associated with general or spinal anesthesia. In general, patients undergoing laparoscopy have no debilitating medical diseases and tolerate the anesthesia better than elderly patients with serious illnesses.

The most frequent complications of laparoscopy occur while creating the pneumoperitoneum; fortunately, most of them are minor and of no consequence. If the Verres needle tip is not in the abdominal cavity, the carbon dioxide will be injected elsewhere. Subcutaneous, omental, and retroperitoneal emphysema are the most common sequelae due to a misplaced needle. Cases of pneumothorax and mediastinal emphysema have also been reported.⁸ These complications are thought to arise from diaphragmatic defects such as developmental anomalies, pathological conditions (e.g., tuberculosis of the diaphragm), or lacerations in the diaphragm resulting from a combination of increased intra-abdominal pressure and diaphragmatic adhesions.

Puncture of a vessel while inserting the Verres needle may lead to hemorrhage or hematoma formation. Rectus muscle hematomas are the most common complication in this group. Severe hemorrhage may necessitate laparotomy, to control bleeding that cannot be controlled with cautery.

Pulmonary air embolism has also been reported⁸ and thought to occur as a result of air being injected directly into a vein. Cardiovascular collapse has also been reported secondary to the development of the pneumoperitoneum. Morison and Riggs¹² report two cases where the heart beat ceased after

approximately two liters of gas had been introduced. These authors hypothesize that CO₂ embolism was the cause for the complications, although they do not rule out the possibility of vagal stimulation as a contributing factor. Blood gas studies have been performed to investigate the consequences of the rapid absorption of carbon dioxide. Siegler¹⁶ has found an insignificant rise in pCO₂ in ten of eleven patients undergoing laparoscopy who were intubated with a cuffed endotracheal tube. The eleventh patient developed multifocal ventricular extrasystoles with a pCO₂ rising from 32.5 to 51.0 mmHg and a corresponding drop in pH from 7.38 to 7.24. Baratz and Karis,² in a study of twenty patients, concluded that "patients undergoing laparoscopy should breathe a gas mixture containing at least fifty percent oxygen, while ventilation is controlled with an endotracheal airway." With spontaneous respiration or intubation with lower oxygen tension, pH and pO₂ fell significantly.

Bowel perforation can occur as a complication of introduction of the Verres needle. This problem is more likely to happen when adhesions are present, and for this reason suspected widespread adhesions from repeated abdominal surgery or from peritonitis are a contraindication to laparoscopy. Because of the small size of the Verres needle and the easy evacuation of bowel gas, bowel perforation with the Verres needle may be of no great consequence.¹¹

Introduction of the trocar itself should carry few risks provided that a satisfactory pneumoperitoneum has been developed. Bowel perforation and hemorrhage are the most serious complications, and when they occur, they often require corrective laparotomy due to the size of the trocar. Similar complications can occur with the laparoscope itself, if this instrument is not handled carefully. Caution should be practiced when investigating cystic masses to avoid the rupture of the viscus. Laparoscopy should be avoided in the presence of a large fluid-filled mass in the abdomen. Incisional hernias and small bowel incarceration have also been reported as a consequence of laparoscopy.^{10,14} Inserting the trocar through a "Z-tract" should minimize the frequency of this problem; nevertheless, careful inspection of the laparoscopy site should follow each procedure. When small bowel incarceration does occur, symptoms may not be manifested until several days after the operation. Infection may complicate any surgical procedure, and peritonitis may result from any bowel perforation.

Laparoscopic tubal cauterization carries all the above risks in addition to other complications resulting from the use of cautery. Hemorrhage is more likely and may be sufficiently severe to require laparotomy. Suppurative salpingitis has been reported as a rare complication.¹ In three cases

occurring in more than 1800 laparoscopic tubal cauterizations reported by Badra et al,¹ there was a delay of at least four days between surgery and the onset of symptoms. In each case an IUD was present prior to surgery and a uterine curettage was performed. Badra suggests that the combined insult of the IUD, curettage and tubal cautery may predispose to suppurative salpingitis. Removal of the IUD several weeks prior to surgery may prevent this complication.

Finally, Thompson and Wheelless¹⁸ report the occurrence of ten bowel burns in a series of 3600 tubal cauterizations. Five of these were immediately recognized, while five others were not diagnosed until after symptoms developed. In the five unrecognized cases, all were readmitted three to seven days postoperatively, all presented with symptoms and signs of pelvic peritonitis associated with ileus and distention, all required laparotomy and bowel resection, and all burns were located in the terminal ileum within two feet of the cecum. These authors suggest that "patients presenting with symptoms and signs of pelvic inflammatory disease associated with ileus and distention following laparoscope sterilization should undergo exploratory laparotomy, if they do not respond within twelve to eighteen hours of medical therapy."

REVIEW OF LAPAROSCOPIES AT THE MAINE MEDICAL CENTER

METHOD OF STUDY

Four hundred and thirty-five laparoscopies at the Maine Medical Center were reviewed in a retrospective manner, beginning with the introduction of the procedure in 1971. All charts were reviewed by the authors.

INDICATIONS FOR LAPAROSCOPY

Of the 435 laparoscopies reviewed in this series, 301 were performed for tubal cauterization, 132 represented diagnostic procedures, and 2 were performed to remove IUD's. The most frequent reasons for diagnostic laparoscopy were abnormal uterine bleeding, pelvic pain, and infertility. Other common indications included the evaluation of pelvic masses and questionable pelvic infections.

Most of the patients were between the ages of 20 and 40 with the ages ranging between 17 to 49. Nearly all the patients were in good health and represented excellent surgical candidates.

RESULTS

The 435 laparoscopies were performed by 13 attending gynecologists and 6 general surgical residents. The attending gynecologists performed 362 laparoscopies and had 29 complications while the residents performed 73 laparoscopies and had 6

TABLE I

LAPAROSCOPIES PERFORMED NOV. 1971-JUNE 1974	
Category of Laparoscopy	Number
A) Sterilization	301
B) Diagnostic	132
C) Fr IUD removal	2
Complications	35

TABLE 2

LAPAROSCOPIC COMPLICATIONS AT MAINE MEDICAL CENTER	
Type	Number
Pain in shoulder or costal margin	11
Subcutaneous Emphysema	2
Uterine perforations	2
Endometriosis at site of tubal cauterization	2
Tender abdomen (etiology not specified in chart)	1
Small rectus hematoma	1
Bleeding from (R) LQ stab wound treated by suture or observation	3
Bleeding from (R) LQ stab wound requiring laparotomy	3
Bleeding into mesentery or transverse colon (minor)	1
Bleeding from (L) fallopian tube during coagulation (requiring laparotomy)	1
Bleeding from adnexal biopsy site — stopped by cautery	1
Broad ligament hematoma	1
1st and 2nd degree skin burn (malfunction of Bovie plate)	1
Burn of ileum requiring laparotomy	1
Postoperative convulsions (patient Dilantin®)	1
Deep thrombophlebitis requiring anticoagulation	1
UTI	1
Urinary retention (patient on Tofranil®)	1

complications. This represents complications rate of 8.01% and 8.21% respectively.

Table 1 shows the number of laparoscopies performed and complications which occurred after 1971. The overall complication rate was 8.04 percent; however, of these 35 cases with complications only a minority resulted in significant discomfort or increased risk to the patient. Table 2 outlines the various complications. Bleeding was one of the most serious problems, necessitating laparotomy to stop the bleeding in four of the eleven cases. Six instances of bleeding occurred when a stab wound was made in a position other than midline (usually hypochondrially). Currently, except in unusual circumstances, both the initial laparoscopic insertion site and any secondary stab wounds are made in the midline. The only other major bleeding complication occurred during a sterilization procedure with bleeding from the left uterine tube and from adnexal biopsy-site which was treated by cautery.

In two of the cases an ectopic insertion site was documented or subcutaneous emphysema occurred postoperatively. Unexplained postoperative abdominal, chest, or shoulder pain complicated eleven procedures. In all cases the pain remitted

spontaneously within two days, and in five cases free air was demonstrated under the diaphragms. In three cases in which spinal anesthesia was used, two developed intraoperative shoulder pain and one patient had persistent hiccoughs. General anesthesia is now employed routinely. The single skin burn occurred when the Bovie ground plate had become dislodged from the patient's thigh; resulting in a 1x2 cm area of first and second degree burns. Since then a pregelled, disposable electrosurgical ground pad; (American Hospital Supply) has been employed. There were two instances of endometriosis occurring postoperatively. The endometriosis occurred at the cauterization sites on the uterine tubes within the first year postoperatively. No endometriosis was seen during the sterilization procedures. We have not seen this complication previously reported in the literature. It may have resulted from sloughing of the cauterized proximal ends of the fallopian tubes with retrograde menstruation. Significantly, there were no deaths in our series. It is interesting to note that 94 patients had a lower abdominal scar prior to the laparoscopy (21.77%). Neither the scars nor adhesions created technique difficulties during laparoscopy.

DISCUSSION

Laparoscopy at the Maine Medical Center has proven to be a useful technique for investigating pelvic disorders and performing female sterilizations. In nearly all cases with pelvic abnormalities either a definite disorder was found or a remediable organic cause for the patient's discomfort was eliminated without necessitating laparotomy.

As more experience has accrued with laparoscopic techniques, fewer complications have resulted. In the first six months of 1974, only one episode of significant bleeding occurred and this was controlled with cautery. The decreasing complication rate has been restricted to cases involving tubal cauterization. Diagnostic procedures now have relatively more complications than laparoscopic sterilization, possibly because of the greater variability in operative technique and unexpected findings in these patients. The low rate of problems involving cases performed by house officers attests to the safety with which laparoscopic technique can be taught.

As surgeons become increasingly aware of the possibilities of laparoscopy, perhaps more attention will be focused towards the remainder of the ab-

dominal cavity. In one of the earlier papers on laparoscopy, Ruddock¹³ discusses its uses in terms of the entire abdomen. He specifically mentions as indications for laparoscopy: differential diagnosis, investigations of tumors, obtaining biopsy specimens under direct vision without laparotomy, drainage of abscesses or cysts, and determination of operability of a lesion.

In conclusion, this study shows laparoscopy to be a reasonably safe procedure when used with general anesthesia and with the precautions enumerated earlier in this paper. The technique is readily taught to the experienced surgeon and is adaptable to the operating rooms of most community hospitals.

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Activated Charcoal: A Forgotten Antidote

FRANK H. LAWRENCE, M.D.* and WALLACE R. MCGREW**

Activated charcoal, an agent known since the time of Hippocrates, is one of the most effective yet neglected antidotes available for the treatment of ingested poisons. A suspension of tasteless, odorless activated charcoal can be used for gastric lavage, as a follow-up to induced emesis, or simply swallowed by the patient in the emergency situation adsorbing and thus inactivating many ingested systemic poisons. It is currently recommended as one of the best, least expensive and most practical antidotes available.^{1,2,3,4,5}

Activated charcoal is a product of the destructive distillation of organic substances prepared in such a manner that the charcoal powder has a large adsorbent surface area. This large area allows polar molecules, including anions, cations and non-electrolytes, to be bound to the charcoal's surface via Van der Waals forces. It has been calculated that a 1 ml suspension of charcoal has an adsorbent surface area of approximately 1,000 square meters.¹³ The charcoal is capable of adsorbing a wide variety of chemicals within the gastrointestinal tract, thus preventing their enteric absorption. In addition to poisons, substances such as vitamins, amino acids and sugars may be adsorbed, however, adsorption of these substances produces no ill effect when the charcoal is administered acutely.¹ Activated charcoal has been recommended as an adsorbent for most systemic poisons and effective *in vivo* binding has been established for a number of commonly ingested chemicals.^{1,2,10} The binding of the charcoal-poison complex is not appreciably affected by pH changes and is thus stable throughout the gastrointestinal tract provided that the dose of charcoal is large in relation to the dose of poison.^{1,2,5} Activated charcoal appears to hold chemicals with a greater tenacity than other available adsorbents and previous concerns about elution of chemicals from charcoal appears unfounded.⁵

GENERAL USE

An activated charcoal slurry administered orally following poisoning provides a convenient emergency measure for home, office or emergency room use.

Two initial approaches to the emergency treatment of the acute poisoning episode are generally accepted: induced emesis or gastric lavage. Induced emesis is currently the most acceptable method for

safely emptying the stomach and is the immediate treatment of choice for most cases involving an ingested poison.³ Though it is recognized that only 40% of an ingested poison is recovered by either emesis or lavage, induced emesis is considered less traumatic and more expedient than gastric lavage. Some sources indicate that lavage may be even less efficient than emesis in removing poison due to stomach recesses sequestering contents and thereby making the poison inaccessible to the lavage tube.^{5,9} However, in the unconscious or very lethargic patient use of gastric lavage with a cuffed endotracheal tube in place is necessary in order to minimize the possibility of vomitus aspiration.^{3,9,12} It is left to one's clinical judgment and the demands of the individual patient to determine whether emesis or lavage will be most effective in evacuating the stomach.

Following either induced emesis or gastric lavage (if the lavage substance was not charcoal), charcoal is the next step in the effort to prevent absorption. Oral instillation of an activated charcoal suspension following induced emesis is appropriate in that activated charcoal acts as a gastrointestinal decontaminate to follow-up the induced emesis.^{1,2,7} As an alternative, the charcoal suspension may be used as the lavage fluid with a charcoal slurry being left in the stomach after the final washing is completed.⁶ Lavage with water has been found to be virtually ineffective in barbiturate poisoning because of the very rapid gastrointestinal absorption of the drug. Lavage with an activated charcoal slurry, on the other hand, has been found effective in removing large quantities of the barbiturate.¹⁴

Emergency over-the-phone prescription of two tablespoons of activated charcoal in a glass of water for a conscious patient is generally recommended; emesis can subsequently be induced, via apomorphine (Ipecac is useless *following* activated charcoal ingestion), as soon as the patient arrives at the emergency facility.⁷ Charcoal is a poor adsorbent for caustic alkalis and mineral acids and its use should be avoided with such ingestions.⁵ On the other hand, its potency with respect to adsorption of many other chemical poisons should recommend its use in poisoning episodes where the ingested agent is unknown.

Activated charcoal suspensions do not lose a significant amount of their adsorptive ability for up to one year following preparation.² Concerns that the charcoal might be inactivated by protracted contact with water and consequent adsorption of water molecules appear unfounded.^{4,10} Thus, charcoal

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slurries can be prepared and stored in the home or emergency room well in advance of their intended use, thereby encouraging use in acute poisoning situations.

The so-called "universal antidote" (a preparation containing tannic acid, magnesium oxide and activated charcoal), burnt toast and charcoal tablets are not to be used as substitutes for an activated charcoal slurry. The use of such ineffective compounds in the past may account for the infrequent use of activated charcoal today.^{1,5,7,11}

SPECIFIC USE

A few of the chemical compounds effectively adsorbed *in vivo* by powdered activated charcoal include:^{4,7}

Acetaminophen	Mefenamic Acid
Aconitine	Mercuric chloride
Aspirin	Methyl salicylate
Atropine	Neguvon
Barbital	Nicotine
Chlordane	Pentobarbital
Chloroquine	Phenobarbital
Chlorpheniramine	Phenylpropanolamine
Chlorpromazine	Propantheline
d-Amphetamine	Propoxyphene
Ethchlorvynol	Quinine
Glutethimide	Salicylamide
Hexachlorophene	Secobarbital
Kerosene	Sodium salicylate
Malathion	Strychnine

It is concluded by many toxicologists that activated charcoal is effective to some degree against an even wider spectrum of ingested agents and that use of activated charcoal in other than the above listed acute poisonings is often recommended.^{1,4,5,7,14} As an example, activated charcoal has been recommended as an adsorbent for the endotoxin of paralytic shellfish poisoning.¹⁵ However, it is to be emphasized that the selection of activated charcoal as an antidote should follow at least some consideration of the type of poisoning being treated and, as with any medication, should not be used indiscriminantly.

DOSAGE

It is currently recommended that a preparation of 50 gm of activated charcoal be mixed with 400 ml of sterile water in a 500 ml polyethylene bottle to prepare a charcoal slurry.¹¹ The slurry can then be administered either orally or via nasogastric tube in 100-200 ml doses (5 ml/kg portions). Alternately, 5-6 tablespoons (approximately 20-24 gm) of activated charcoal can be dissolved in a glass of water and swallowed or instilled by nasogastric tube.^{1,9} Massive doses of activated charcoal (up to 100 gm) have been well tolerated orally.⁵ The dose of activated charcoal must be between five and ten times the estimated dose of poison in order to achieve therapeutic levels.⁵ A cathartic such as sodium sul-

Continued on Page 313

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdose or individual hypersensitivity, reactions similar to those after meperidine or morphine overdose may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or Narcan® (naloxone HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdose; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdose: Keep the medication out of the reach of children since accidental overdose may cause severe, even fatal, respiratory depression. Signs of overdose include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

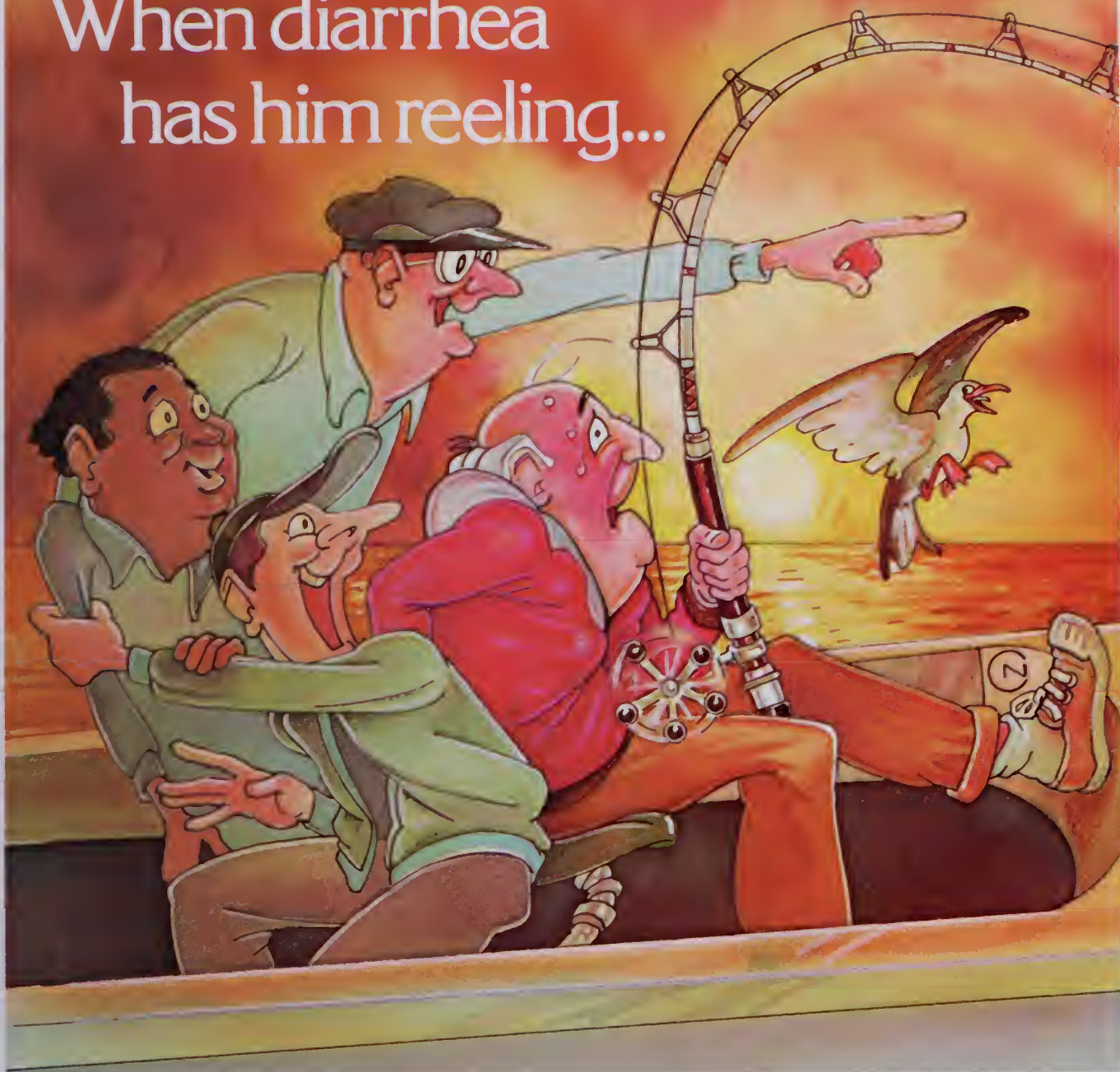
Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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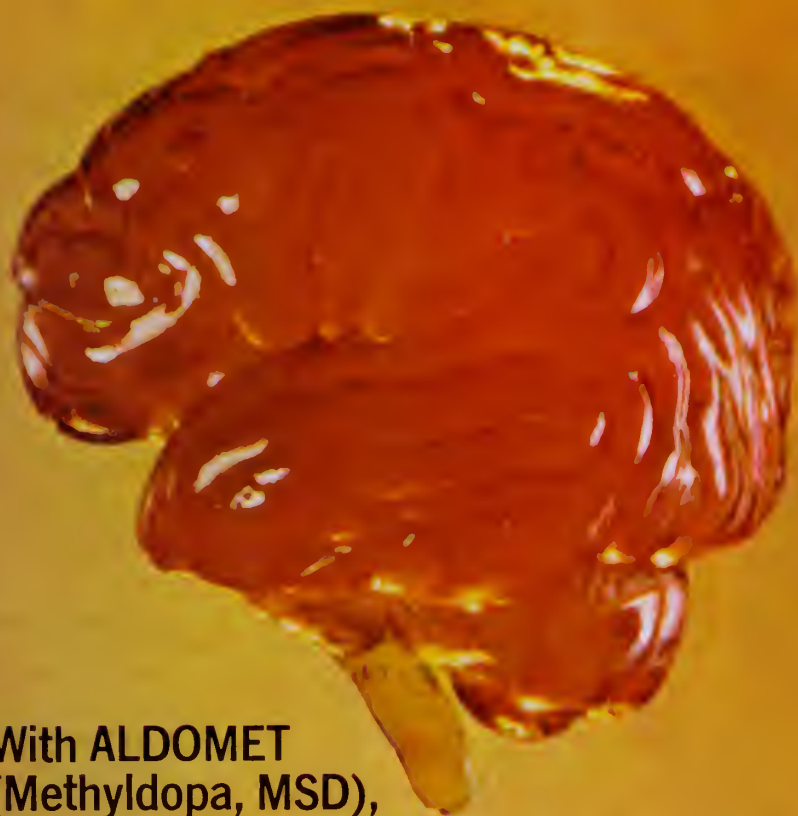


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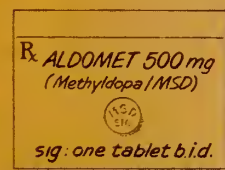
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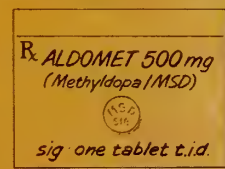
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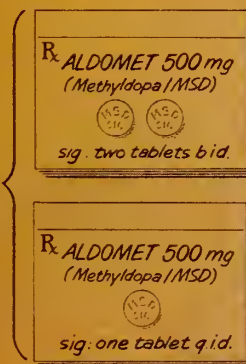
1.0-g
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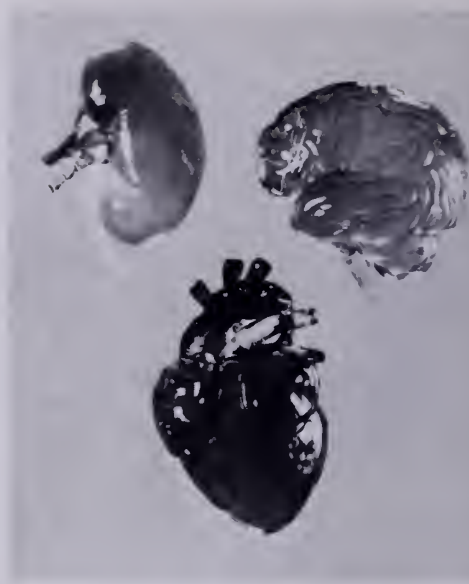
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Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyldopa therapy has been associated with liver disorders (see Warnings); hypersensitivity.

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With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or

cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

Use in Pregnancy: Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: *Central nervous system:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetotic movements; psychic disturbances, including nightmares and reversible mild psychoses or depression.

Cardiovascular: Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear.)

Gastrointestinal: Nausea, vomiting, distention, constipation, flatus, diarrhea, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis.

Hepatic: Abnormal liver function tests, jaundice, liver disorders.

Hematologic: Positive Coombs test, hemolytic anemia, leukopenia, granulocytopenia, thrombocytopenia.

Allergic: Drug-related fever, myocarditis.

Other: Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, dermatologic reactions including eczema and lichenoid eruptions, mild arthralgia, myalgia.

Note: Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third month of therapy; increased dosage or adding a thiazide frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

How Supplied: Tablets, containing 125 mg methyldopa each, in bottles of 100; Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000. Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

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fate (10-30 gm), orally or via nasogastric tube, is recommended as a means of speeding movement of the poison-charcoal complex and any remaining unbound poison through the intestine.^{3,4,9,12} Contraindications to gastric lavage are ingestion of a strong corrosive agent or ingestion of liquid hydrocarbon. If the patient is comatose or convulsing, a cuffed endotracheal tube should be placed prior to lavage.^{5,12} No additives should be placed in the activated charcoal suspension as they will be adsorbed thus inactivating the charcoal and the additive. Not all activated charcoal preparations on the market are equally effective and AC-Merck, Nuchor C and Norit A are frequently recommended brands because they have been found to have approximately 35% greater adsorbing capacity than some other brands, i.e., Darco G-60.²

CONCLUSION

Activated charcoal is an excellent choice of adsorbent antidote for most episodes of poisoning by ingestion. If available in the home or emergency room as either a pre-mixed preparation or powder form, an activated charcoal suspension can serve as a gastric lavage fluid or as an adjuvant to emesis to aid in gastrointestinal decontamination. In the past, activated charcoal slurries have often been neglected because of the time consuming and messy task entailed in emergency preparation. Consequently, this inexpensive but markedly effective antidote for the immediate treatment of poisoning has been relegated to an obscure place on the medication shelf.^{1,5,7} Hopefully, ready-to-use charcoal suspensions will be prepared by medical institutions or commercial firms in an effort to promote more widespread use of this neglected antidote.^{2,7,15}

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Angiographic Demonstration of Critical Arteriosclerotic Lesions of the Carotid Bifurcation

L. REED ALTEMUS, M.D.*

Clarifying the nature and hemodynamic effect of arteriosclerotic lesions of the extracranial carotid arteries is essential in the evaluation of transient or progressing ischemic neurological deficits (TIA's). Arteriography remains the best method of establishing the relationship between extracranial occlusive disease and clinical signs of cerebral ischemia. In 1856, Virchow described the first case of visual loss secondary to carotid artery thrombosis.⁷ Subsequently, Chiari in 1905 correlated thrombosis of the cervical internal carotid with intracranial embolization.² Since these historic reports, our understanding of the pathophysiology of cerebrovascular occlusive disease has advanced considerably but many questions remain unanswered. Two such issues concern the need for comprehensive angiography (four-vessel) in evaluating all patients with transient ischemic attacks and whether the risk involved with selective carotid arteriography is justified. The 1968 Joint Study of Extracranial Arterial Occlusion concluded that not only is four-vessel angiography achieved with an acceptable complication rate** but is "essential for the clear understanding of the causal mechanisms responsible for the production of signs and symptoms in individual patients."⁴ More recently Roberson et al demonstrated the advantage of transfemoral selective carotid catheterization for more detailed visualization of stenotic lesions especially those containing mural thrombi.⁶ It is the purpose of the following report to further emphasize the advantage of retrograde femoral artery catheterization of the common carotid arteries with visualization of both the extracranial and intracranial circulation in patients with transient neurological disturbance.

APPEARANCE OF CRITICAL LESIONS AT THE CAROTID BIFURCATION

Uncomplicated† Stenosis: Pure arteriosclerotic stenosis of the extracranial carotid arteries is a recognized cause of transient neurological disturbance (Fig. 1). The degree of stenosis necessary to



Fig. 1. Common carotid angiogram demonstrating tight (2 mm.) stenosis of the internal carotid artery.

produce clinical symptoms remains a controversial subject. Some investigators claim 50 percent stenosis of the internal carotid significant³ while others feel 80 percent is required.⁵ Determining the absolute cross-sectional area of constriction has been proposed and residual lumens of 2-4 sq. mm. were found to alter flow or produce detectable pressure gradients.¹ Other factors such as length of stenosis, number of vessels involved, the anatomy of the circle of Willis, and the status of the opposite cervical carotid determine the ultimate hemodynamic effect of unilateral carotid stenosis. These parameters are best evaluated by four-vessel comprehen-

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**Overall grave complication rate of 1.2 percent.

†Unassociated with ulceration or thrombus.

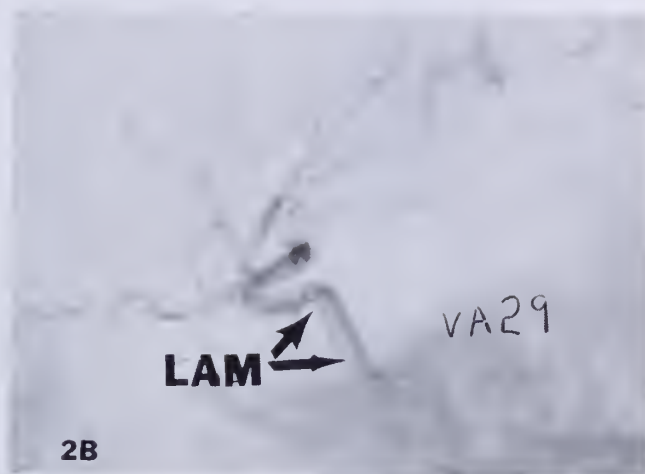
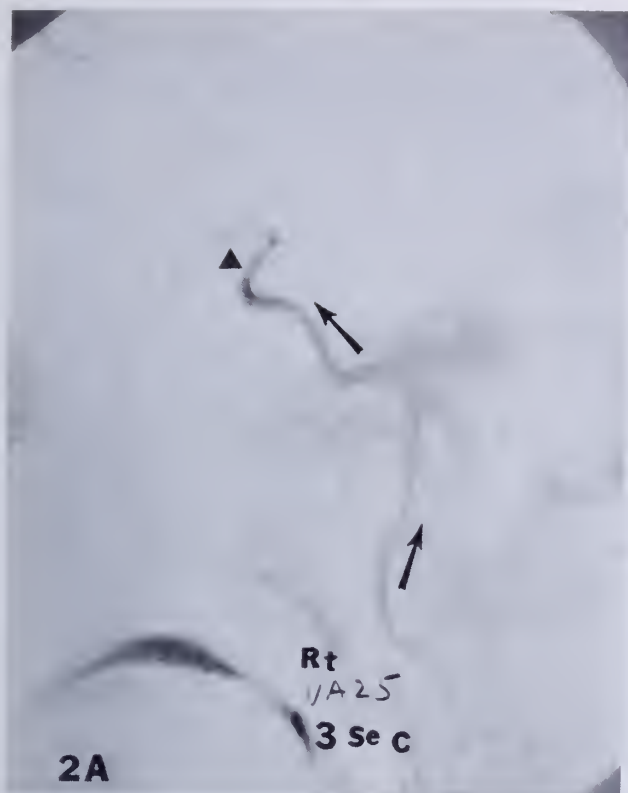


Fig. 2. Angiographic examples of the hemodynamic effect of tight extracranial carotid stenosis. A. Proximal extracranial stenosis causing slow flow within internal carotid artery. Three seconds after injection the internal carotid including its supraclinoid portion (arrow head) remains filled indicating extremely slow blood flow. B. Proximal extracranial stenosis causing slow laminar type flow within the internal carotid artery.

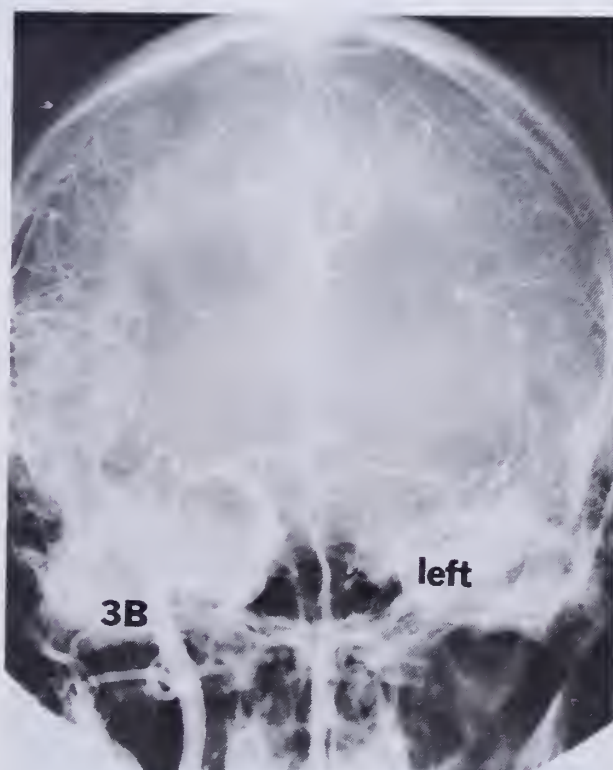
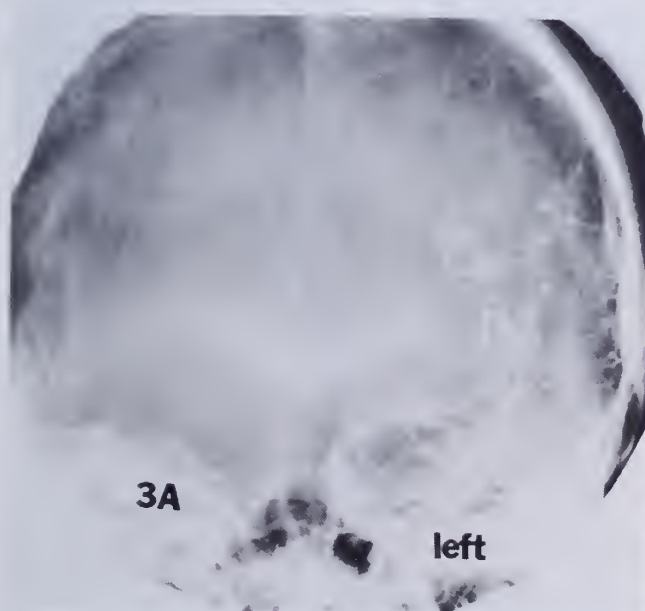


Fig. 3. Angiographic evaluation of the circle of Willis. A. Absence of left anterior cerebral artery above a tight extracranial right carotid stenosis indicating absence of anterior collateral flow potential from left hemispheric circulation. B. Patent anterior communicating artery with cross filling to opposite hemisphere above a tight left carotid stenosis. Example A thus a more dangerous hemodynamic situation than B where cross hemispheric filling is available.



Fig. 4. Angiographic demonstration of internal carotid artery stenosis with atherosclerotic ulceration (arrow).

sive selective angiography of both the extracranial and intracranial circulation (Figs. 2 and 3).

Stenosis With Ulceration: Ulceration of atherosclerotic plaques is a source of embolic material and thus a potential cause of transient ischemic attacks. Tight stenosis poses the risk of subsequent complete occlusion if a mural thrombus develops or further hemorrhage into the ulcerating plaque obliterates the residual lumen (Fig. 4).

Intraluminal Mural Thrombus: Mural thrombus existing at the site of carotid stenosis (Fig. 5A) or superimposed on severe atherosclerotic disease (Fig. 5B) is a potential dangerous circumstance. Propagation of the intraluminal thrombus may eventually result in total occlusion or serve as a source of cerebral embolization. Ten percent of stenotic carotid disease is associated with mural thrombi which are demonstrable by selective common carotid angiography.⁶

Total Carotid Occlusion: Total carotid occlusion either of the common or internal carotid occurs without clinical sequelae in approximately 15 percent of instances. An old or long standing occlusion is angiographically recognized by a bullet nose or blunt appearance at the occlusion site (Fig. 6A) while acute occlusion, on the other hand, appears



Fig. 5. Angiographic appearances of mural thrombi. A. Filling defect (arrow) within lumen of internal carotid artery above common carotid stenosis. B. Intraluminal thrombus (arrow) attached to surface of arteriosclerotic plaques of internal carotid artery (arrow).

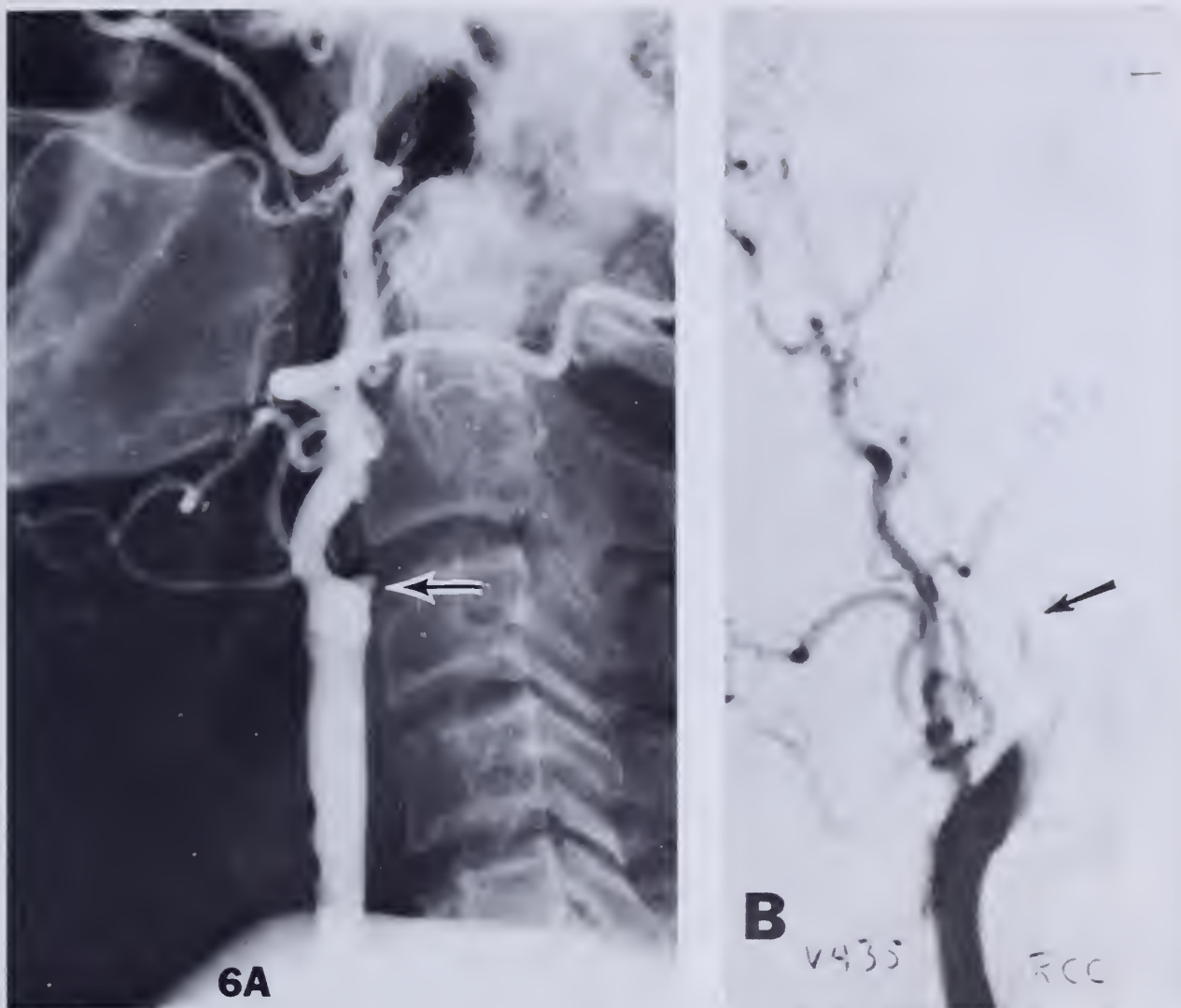


Fig. 6. Angiographic appearance of total internal carotid occlusion. A. Blunt appearance (arrow) indicating old occlusion. B. Tapered appearance of acute occlusion.

more pointed or tapered (Fig. 6B). Transient neurological ischemic attacks may continue after complete occlusion of the cervical carotid. When the ipsilateral hemisphere above the occluded carotid is clinically implicated as the site of persistent cortical ischemia, four-vessel comprehensive angiography is extremely valuable, and may demonstrate the possible cause of persistent symptoms. The cause may be hemodynamic if other extracranial stenotic lesions exist or embolic if distal portions of the occluded carotid are re-constituted by sluggish flow from collateral sources (Fig. 7). Segments kept patent by collateral flow above a totally thrombosed lumen continue to serve as a locus for further thromboembolization.

SUMMARY

The types of extracranial arteriosclerotic lesions

which intermittently impair cerebral blood flow are reviewed. Their hemodynamic effect, potential for total occlusion and/or embolization is discussed. The author believes that these parameters are best assessed by comprehensive selective common carotid angiography which visualizes both the extracranial and intracranial circulation.

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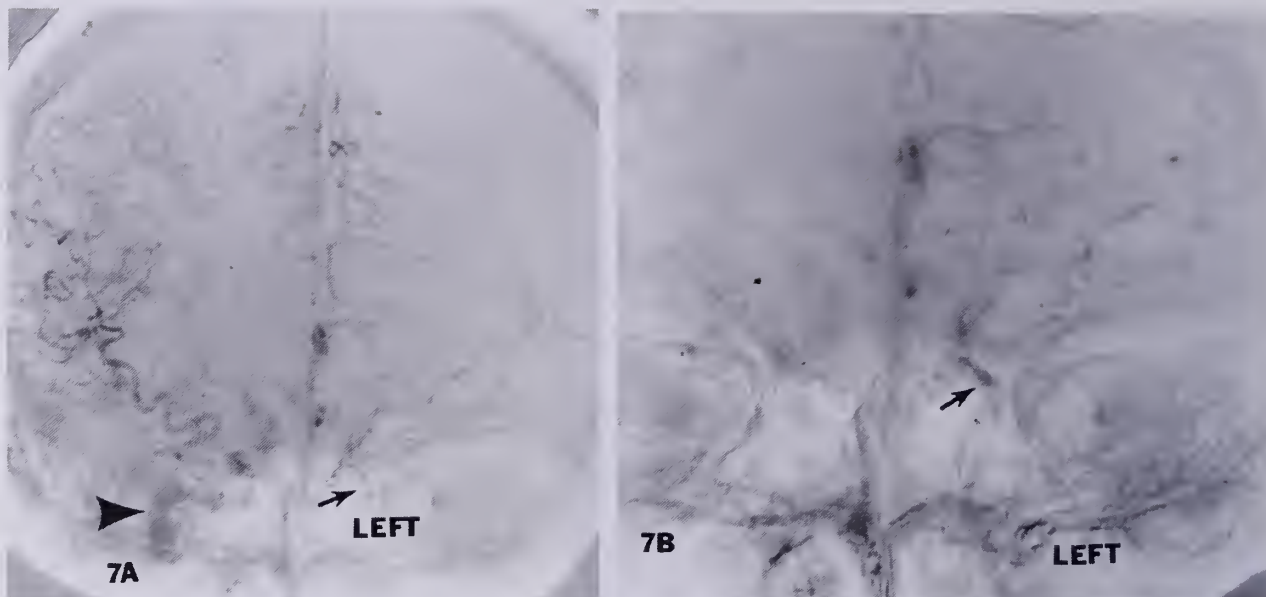


Fig. 7. Re-constitution of the distal intracranial portion of a completely occluded extracranial carotid artery. A. The left extracranial carotid is occluded but cross filling from the right carotid circulation re-constitutes the left ophthalmic artery (arrow). B. Seconds later the re-constituted left ophthalmic artery fills the intracranial portion of the left carotid artery. This re-constituted segment containing sluggish flow serves as a possible cause of cerebral thromboembolization, or persistent transient monocular blindness.

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Silent Aneurysm

CHARLES E. DIXON, M.D.

Arterio-arterial embolization, as an entity, has been found to play an increasingly important role in peripheral ischemia. The symptom complex of transient ischemia attacks and the visualization of the tiny cholesterol crystals in the retinal arteries associated with ulcerated plaques at the bifurcation of the carotid artery are well known. Miles et al¹ have reported observations suggesting that small emboli occur to the coronary circulation which could come from ulcerated plaques ultimately resulting in diffuse myocardial fibrosis. Sudden onset of toe or foot ischemia with intact distal pulses, the "blue toe" syndrome, has been recognized as due to emboli originating in the aortic or iliac vessels. Periodically, authors report peripheral emboli beyond aneurysms.

We have seen four cases of unsuspected abdominal aortic aneurysm as a cause of peripheral vascular occlusive disease. This report is designed to emphasize the significance of arterial embolization, especially from abdominal aortic aneurysms and to discuss its incidence and treatment.

CASE REPORTS

CASE #1: Case History: A 73-year-old white male gave a three-week history of rather severe itching in his left first, second, and third toes. This was accompanied by a violaceous discoloration of the toes without tenderness. Examination revealed multiple petechiae over the first, second, and third toes bilaterally. Abdominal examination revealed a 5 cm. in diameter abdominal aortic aneurysm which was non-tender. At aneurysmectomy, the patient was found to have fresh thrombus, thrombus of slightly older duration, and organized thrombus along the walls of the aneurysm (Fig. 1). His feet are presently asymptomatic, post aneurysmectomy.

CASE #2: Case History: A 74-year-old white male with a three-year history of progressive claudication in both calves. The patient had had a cold injury to both feet in the past which caused the patient to lose both great toes and the left second toe. One month prior to being seen, he developed pain in the right fourth and fifth toes with bluish discoloration. Examination confirmed mild cyanosis of the right fourth and fifth toes with 2+ right femoral and popliteal pulses. Blood pressure at the right ankle was 174/ and 128/ systolic in the dorsalis pedis and posterior tibial arteries respectively although they could not be felt. Examination of the abdomen revealed a 6 cm. in diameter, non-tender abdominal aortic aneurysm. At aneurysmectomy, the patient was found to have fresh thrombus lining the wall of the aneurysm. His right foot has become asymptomatic.

CASE #3: Case History: A 74-year-old white male with sudden onset of left calf claudication and tenderness in his left calf. Examination revealed no pulses below the left popliteal fossa. A 5 cm. in diameter mildly tender abdominal aortic aneurysm was palpable. At aneurysmectomy, the patient was found to have fresh thrombus lining the walls of the aneurysm. At a later operation, organized thrombus was found at the trifurcation of the popliteal artery. The anterior tibial artery was opened by

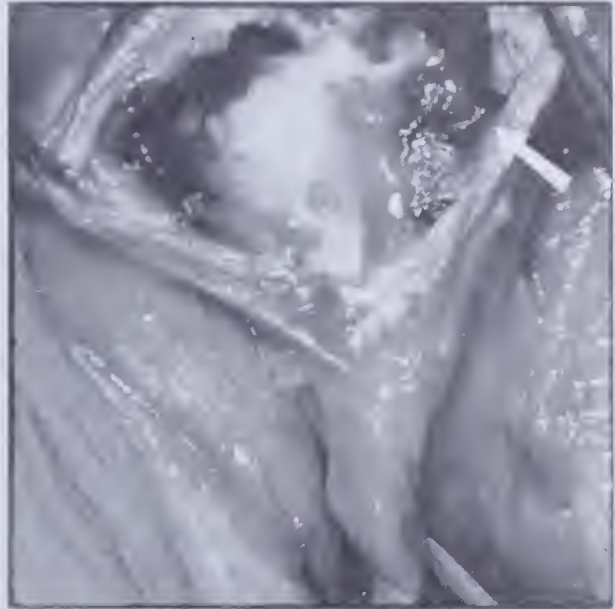


Fig. 1. The arrow indicates heaped up thrombus, both fresh and somewhat older, lining the walls of the abdominal aortic aneurysm in Case #1.

thrombectomy and endarterectomy restoring a satisfactory distal pulse.

CASE #4: Case History: A 72-year-old white male developed the sudden onset of claudication of the left leg six months prior to being seen and which had been stable. Examination revealed no pulses beyond the left femoral pulse and a 4-5 cm. in diameter abdominal aortic aneurysm which was mildly tender. At aneurysmectomy, considerable fresh thrombus was found. It is hypothesized that this patient embolized to the adductor hiatus. The patient's claudication does not incapacitate him, nor does it change his life style.

DISCUSSION

A review of the literature reveals very little in regard to aneurysmal embolization. Edwards and his associates² discuss, in detail, 82 patients with proven peripheral arterial embolization. Ninety-four percent arose within the heart and three were associated with atherosclerotic ulcerations of the aorta. Darling, Austin, and Linton³ recorded a ten-year experience with 260 patients experiencing 426 arterial emboli. In four patients (1.5%) the source of emboli was from a mural thrombus within an abdominal aortic or iliac aneurysm. Crane⁴ reported on three patients in 1967 with peripheral arterial embolization with atherothrombi from aorto-iliac aneurysm. His presentation focused on digital ischemia and gangrene in the presence of one

or two palpable pedal pulses. Lord et al⁵, at Beth Israel Hospital in New York City, reported a four-year study with 39 of 133 patients subjected to resection of an aortic aneurysm who were demonstrated to have embolization to the lower extremities. Their conclusion was that a principle hazard to a patient with an abdominal aortic aneurysm is embolization distally, probably more commonly than frank rupture. They suggested that all patients with arterial occlusive disease of the lower extremities have complete aorto-peripheral angiographic studies.

The pathogenesis of arterial embolization seems to be an ulceration of an atherosclerotic plaque within the thoracic or abdominal aortic or iliac vessels. This ulcerated plaque becomes covered with platelets or thrombi and emboli of this substance as well as possible atherosclerotic debris are intermittently dislodged distally. How frequently this occurs is not known at this present time. Repeated embolic episodes may be frequent and at times recovery probably is almost complete; although, in other patients, progression of ischemia must occur, ultimately terminating in loss of limb.

The most striking clinical appearance of the distal emboli is the "blue toe" syndrome. This represents severe ischemia of the toes or portions of the feet frequently bilaterally and is associated with renal failure. Before the pathogenesis was understood, the diagnosis remained unknown. Pulses frequently remained palpable even while distal ischemia progressed even to gangrene.

Episodes of cerebral vascular ischemia in combination with neurological symptoms which are fleeting or transient are typical of emboli from ulcerated plaques within the carotid bifurcation. In the upper extremity, the subclavian artery is the most frequently involved vessel with distal embolization causing repeated attacks simulating Raynaud's phenomenon.

The diagnosis should be suspected from a finding of severe ischemia of a digit with palpable pulses, sudden onset of claudication or, petechial hemorrhages. Determination of the source of the emboli is extremely important as frequently this condition can be corrected surgically, often by a simple endarterectomy. Detailed angiographic studies are necessary for this, as might be imagined.

In this series of four cases, it was felt that the treatment should be by early aneurysmectomy as

the potential for re-embolization was great at any time. It was felt that systemic anticoagulation was of some risk especially in the one patient with an expanding aortic aneurysm and preparations were made rapidly for elective aneurysmectomy on a semi-emergent basis. Treatment of the peripheral embolization, it was felt, should be done at the time of aneurysmectomy if at all possible; although, it was not felt that the treatment of the peripheral disease was necessary at the time of the aneurysmectomy if the limb was viable and not threatened by pregangrenous ischemia. It was also felt that primary treatment of peripheral embolization without treatment of the aneurysm would expose the patient to the risk of re-embolization perhaps to the other limb or the same limb destroying the potential benefits of the embolectomy or perhaps distal reconstruction. If the limb was threatened by ischemia, however, treatment must be directed to limb salvage primarily with repair of the aneurysm at the same time or as soon as possible.

Classically, the indication for abdominal aortic aneurysmectomy is a pulsatile mass which will, in a high percentage of cases, go on to spontaneous rupture. It is felt that peripheral embolization from abdominal aortic aneurysms is indeed a significant factor in this disease and is another indication for early aneurysmectomy.

SUMMARY

Four cases of peripheral embolization from an abdominal aortic aneurysm are presented. In all cases, the presence of the aneurysm was unsuspected by the referring physician. This article emphasizes the significance of arterio-arterial embolization and the importance of determining its origin.

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498 Essex Street, Bangor, Maine 04401



Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

- Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
- Can relieve nausea and vomiting often associated with vertigo.*
- Usual adult dosage for Antivert/25 for vertigo*: one tablet t.i.d.
- Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
- Antivert/25 (meclizine HCl) 25 mg. *Chewable* Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg/kg/day in rabbits and 10 mg/kg/day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.


Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

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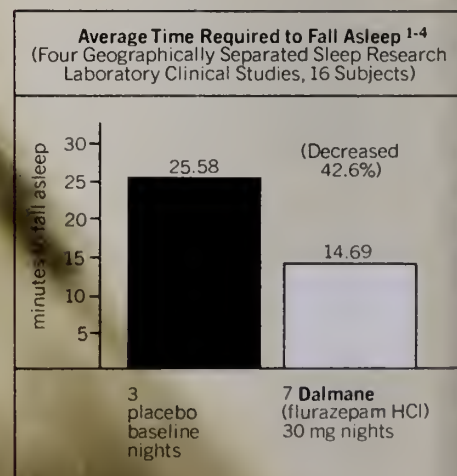
Antivert[®]/25 (meclizine HCl) 25 mg. Tablets for vertigo*



How do you handle trouble falling asleep?

With Dalmane® (flurazepam HCl), results are highly predictable.

As demonstrated below, Dalmane induces sleep within 17 minutes, on average:¹⁻⁴



And for those with trouble staying asleep or sleeping long enough...

...sleep research laboratory clinical studies prove: Dalmane decreases number of nighttime awakenings and increases total sleep time.⁵

Dalmane (flurazepam HCl) is relatively safe, seldom causes morning "hang-over"

Dalmane is generally well tolerated. The usual adult dose of 30 mg should initially be lowered to 15 mg for the elderly and debilitated, to help preclude oversedation, dizziness or ataxia. Appraisal of possible risks is suggested before prescribing.

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4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
5. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

Before prescribing Dalmane (flurazepam HCl), please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly

or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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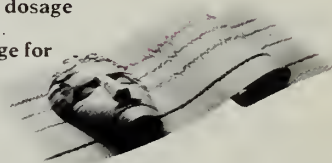
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- sleep within 17 minutes, on average
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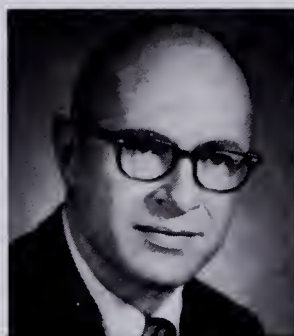


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Nutley, New Jersey 07110

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

main purpose of drug information for the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with this agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a long one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005



Health Care and the 107th Maine Legislature

CHARLES L. CRAGIN III, Esquire*

Historically, effective democracy has implied the existence of an opportunity for the public or its elected representatives to make informed choices. Informed choice necessitates a clear understanding of the facts. After 109 days of legislative activities, the Regular Session of the 107th Maine Legislature adjourned on July 2, 1975. It left in its adjournment wake the statutory indicia of its attempt to make informed choices on a broad range of subjects relating to the health care of Maine citizens. Some of these laws became effective immediately upon passage while most floated in the legislative limbo until October 1, 1975. While some might argue that some of these laws resulted from a misunderstanding of the facts or a lack of knowledge on the part of the lawmakers, it continues to become increasingly clear that the members of the Maine Legislature will deal with these sophisticated issues. Thus, it is incumbent upon both the professional providers of health care and the consumers of such services to provide the elected representatives with the facts upon which to make these important choices.

While most health care issues do not carry with them the necessary glamour required for press coverage and reportorial essays, the Maine Legislature dealt with a significant number of matters either directly or peripherally affecting the health care of the citizens of Maine. It is not the purpose of this article to definitively discuss each piece of legislation. Rather, the article attempts to bring to the reader's attention many of the changes in Maine law with which a person involved in the health care field should be aware.

CHILD ABUSE

After several months of tedious work and many heated debates, the Joint Standing Committee on Human Resources, chaired by Senator Bennett

Katz of Augusta and Representative Gerald Talbot of Portland, reported to the floor legislation designed to revise the State's laws relating to child abuse in a manner which would make Maine eligible for federal grants. The legislation, which became effective on April 21, 1975, expanded the definition of "child abuse and neglect" to mean "the physical or mental injury, sexual abuse, negligent treatment or maltreatment of a child under the age of 18 years of age by a person who is responsible for the child's welfare under circumstances which indicate that the child's health or welfare is harmed or threatened thereby."

The law placed a mandatory duty upon various professionals, including physicians, dentists, nurses, and teachers, to immediately report to the Department of Health & Welfare when the person "knows or has reasonable cause to suspect that a child has been subjected to abuse or neglect or observes the child being subjected to conditions or circumstances which would reasonably result in abuse, when such person is acting in his professional capacity. . . ." While guaranteeing immunity, both civil and criminal, to persons making such reports, the law imposed a criminal fine of \$200 for failure to report. The law does, however, specifically provide that such a conviction could not be used "as a basis for termination of employment or for suspension, revocation or non-renewal of a professional license."

MALPRACTICE INSURANCE

The Legislature, at the primary direction of Senator Gerard P. Conley of Portland, Senator Hayes Gahagan of Caribou and Representative Louis Jalbert of Lewiston, took positive steps to avert the anticipated "malpractice insurance crisis" on both a short-term and long-term basis. Utilizing a legislative vehicle originally introduced by Representative Lawrence Connolly of Portland, the Legislature enacted the "Maine Medical and Hospital Malpractice Joint Underwriting Association Act" which became effective as an emergency on June 11, 1975. This legislation authorized the establishment of a temporary joint underwriting association of all insurers authorized to write personal injury liability insurance in Maine.

The expressed purpose of the Association is "to provide for a period not to exceed two years, a market for medical malpractice insurance on a self-supporting basis. . . ." The Association is not authorized to commence operation until the Super-

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Mr. Cragin serves as legislative and legal counsel to the Maine Medical Association and the Maine Hospital Association and legislative counsel to Maine Blue Cross and Blue Shield.

intendent of Insurance has determined that medical malpractice insurance is not readily available in the voluntary market. The Association is to be governed by 11 directors, eight of whom shall be insurance industry representatives. Of the remaining three directors, two are to be representatives of the Maine Medical Association and one is to represent the Maine Hospital Association.

Recognizing that an underwriting association is only a measure of interim relief, Senator Conley and Senator Gahagan introduced legislation proposing the establishment of a special commission to prepare legislation to "insure the availability of medical and hospital malpractice insurance to physicians and hospitals throughout the State and to develop a more equitable system of relief for malpractice claims." Speedily handled by the Joint Standing Committee on Health and Institutional Services, chaired by Senator Walter W. Hichens of Eliot and Representative Harlan C. Goodwin, Jr. of South Berwick, the legislation was signed into law by the Governor on June 3, 1975 and the Commission is now in the formative process.

Due to the fiscal situation of State government, the Health and Institutional Services Committee recommended that the operating costs of the Commission should be borne by the Board of Registration in Medicine and the Board of Osteopathic Examination and Registration. The Commission composition presents a wide variety of expertise and viewpoints and will be chaired by a sitting or retired justice of the Maine Supreme Judicial Court. Also serving on the Commission will be representatives of the Maine Hospital Association, Maine Medical Association, Maine Osteopathic Association, Maine Bar Association, and Maine Blue Cross and Blue Shield. The Commission is required to submit its proposal to the Legislature no later than January of 1977.

PEER REVIEW

In the field of peer review, the Legislature took action upon the recommendations of Representatives John McKernan of Bangor, Olympia Snow of Auburn, Richard Carey of Waterville, and Harlan Goodwin of South Berwick that physicians be encouraged to participate in peer review activities. Following their recommendations, the Joint Standing Committee on Judiciary, chaired by Senator Samuel W. Collins, Jr. of Rockland and Representative Roland A. Gauthier of Sanford, reported out legislation which received approval by the Legislature and became effective on October 1, 1975. Under this legislation, allopathic physicians are immune from civil liability "as a result of his acts, omissions or decisions in connection with his duties on a utilization review committee, medical review committee, surgical review committee, peer

review committee or disciplinary committee which is a requirement of accreditation by the Joint Commission on Accreditation of Hospitals or is established and operated under the auspices of the physician's respective State or county professional society or the Board of Registration in Medicine." Osteopathic physicians were granted civil immunity with regard to participation on utilization review or peer review committees and dentists were granted immunity with regard to peer review activities.

Acknowledging the necessity for confidentiality of review proceedings in order to foster candid discussion, the Judiciary Committee favorably reported legislation designed to insure that the proceedings and records of proceedings of medical staff reviews and hospital reviews "conducted by committees of physicians and other health care personnel on behalf of hospitals located within the State" would be confidential and exempt from discovery "without a showing of good cause." In order to enjoy the confidential status, the reviews must be required by State or federal laws or regulations or as a condition of accreditation by the Joint Commission on Accreditation of Hospitals or the American Osteopathic Association on Hospital Accreditation.

DRUGS

Prescription, Sale, Administration

As the result of legislation originally introduced by Senator Conley of Portland and Representative Harold R. Cox of Brewer, prescription forms in the State of Maine *must* be changed by January 1, 1976. After a substantial amount of work by the Health and Institutional Services Committee and much input by physicians, pharmacists, and pharmaceutical manufacturers, the Legislature enacted legislation requiring every written prescription issued by a Maine physician, osteopath, or dentist to contain a box at least ½ inch by ½ inch in the lower right-hand corner of the prescription form. To the left of this box, the following words *must* appear:

"Any drug which is the generic or chemical equivalent of the drug specified above in this prescription may be dispensed provided that the drug dispensed is listed in the current edition of either the National Formulary or the United States Pharmacopeia and provided that no check mark (✓) has been handwritten in the box in the right-hand lower corner."

If the prescriber fails to check the box, a pharmacist is authorized to substitute. However, the pharmacist must advise the customer of the substitution and may not substitute a drug which has a price in excess of the price of the drug specified by the prescriber.

The Conley/Cox team also proposed legislation

which, as of October 1, 1975, *permits* pharmacists to advertise certain prescription drugs. This law also *requires* pharmacies to conspicuously post a list of the 100 prescription drugs "sold most frequently in the State during the previous year. . . ."

Resolving a controversy between some ophthalmologists and some optometrists, the Legislature authorized qualified optometrists to utilize topical anesthetics and mydriatics for diagnostic purposes. Before utilizing diagnostic drugs, an optometrist must secure a diagnostic drug license.

Overriding a gubernatorial veto, the Legislature placed on the books legislation originally sponsored by Senator Walter Hichens which places additional duties on pharmacists and pharmacies. Labelled as a means of providing Maine citizens with "Uniform Quality Pharmaceutical Health Care," the law requires each pharmacy to maintain a "patient profile record system" which can be immediately retrieved. With limited exceptions, the law also requires that pharmacists "must *orally* explain to the patient or the patient's agent, the directions for use and any additional information, *in writing if necessary*, to assure the proper utilization of the medication or device prescribed."

Responding to a request from Governor James Longley, the Legislature enacted legislation authorizing the Department of Health and Welfare to "provide free prescription and non-prescription drugs and medication to disadvantaged, elderly individuals." Financing of the program is severely limited, however, with the Legislature appropriating \$2.00 from the General Fund for the biennium "to carry out the purposes of this Act."

THIRD PARTY BENEFITS AND PAYMENTS TO PROVIDERS

The 107th Legislature saw escalating requests by various interest groups, including professional providers, for the Legislature to mandate various categories of coverage provided by commercial insurers and Blue Cross-Blue Shield. The first to see the light of legislative enactment was an act expanding the scope of compensatory activities by a chiropractor for services provided to a Workmen's Compensation recipient. This legislation, introduced by Representative Kathleen Watson Goodwin of Bath, authorized Workmen's Compensation insurers to pay for x-rays conducted by chiropractors and for examination and treatment relating to a "lumbar, sacral, dorsal or cervical subluxation. . . ."

The Joint Standing Committee on Business Legislation, chaired by Senator John Thomas of Waterville and Representative Nancy Clark of Freeport, was called upon to examine proposals for maternity benefits for single women and minor dependents and coverage for neonates. With unanimous reports

and minimal debate, the Legislature ordered all commercial insurers and Blue Cross to provide the same maternity benefits to single women and minor children as had been provided to married women and to provide coverage for children from the moment of birth if coverage was provided for family members.

Proposals by dentists and psychologists under the "Freedom of Choice" banner were more difficult to deal with. However, passage was finally achieved of a proposal requiring commercial insurers and Blue Cross to pay dentists for services performed by them if such services would have been covered had they been performed by a physician. A substantial amount of debate was engendered in the Legislature with regard to a proposal requiring commercial insurers and Blue Cross to pay or reimburse for "mental health services" provided by a psychologist if such services would have been covered if provided by another health care professional. Following an Attorney General's opinion that the original legislation would authorize psychologists to practice medicine, the legislation was amended and received final passage.

PHYSICAL EXAMINATIONS BY DENTISTS

Dentists came before the Committee on Health and Institutional Services with a legislative proposal authorizing them to conduct physical examinations without limitation. As enacted, however, the law authorizes dentists to "take case histories and perform physical examinations to the extent such activities are necessary in the exercise of due care in conjunction with the provision of dental treatment or the administration of general or local anesthetics." The law does not authorize such activities in a hospital unless permitted by the hospital.

HEALTH MAINTENANCE ORGANIZATIONS

Following a year of study by the Health and Institutional Services Committee, legislation introduced by Representative Richard G. Morton of Farmington authorizing the establishment of Health Maintenance Organizations was enacted. This comprehensive legislation authorizes any person to establish an HMO and provides for registration and review by the Superintendent of Insurance and the Commissioner of the Department of Health and Welfare.

MAINE HEALTH FACILITIES AUTHORITY

In an effort to expedite the operations of the legislatively established Maine Health Facilities Authority in the issuance of bonds to finance hospital projects, the Legislature removed the requirement that the Governor and Executive Council conduct hearings and issue its approval prior to the issuance

of any bonds. At the suggestion of Representative John L. Martin of Eagle Lake, Speaker of the House, the Legislature authorized the Authority to make its own determinations as to need, feasibility, etc. of a project.

CONSUMER REPRESENTATION

After several years of discussion and with the endorsement of most professional societies, including the Maine Medical Association, the Legislature placed into law a requirement that all professional and occupational licensing boards have at least one "public member."

MEDICAL LABORATORIES

During the session the Health and Institutional Services Committee completed a major revision of the laws relating to medical laboratories. The act which became effective on May 5, 1975, retained the exemption of prior law relating to hospitals and physicians. However, it removed the requirement that the owner of a laboratory as well as the director have special qualifications. The act also created the "Maine Medical Laboratory Commission" composed of 10 members including one representative of the Maine Medical Association and one representative of the Maine Osteopathic Association. The Commission is required to consult with the Department of Health and Welfare on matters of policy affecting the administration of the law and in the development, revision and enforcement of rules and regulations promulgated under the law.

The Legislature also placed the Diagnostic Laboratory of the Department of Health and Welfare on a fee-for-service basis by requiring that the laboratory "charge the average costs for certain services rendered." Exempt from the charge system are services "considered to be essential to the maintenance of the public health. . . ."

AMBULANCE PERSONNEL

Physicians involved in emergency room activities expressed concern that ambulance personnel were not authorized by existing law to continue to render emergency treatment once a patient had been delivered to a hospital but while awaiting attention. As a result of this concern, Representative Neil Rolde of York proposed legislation which, as of October 1, 1975, authorizes ambulance personnel to continue emergency treatment of a patient after arrival at a hospital "under the direction and control of a physician or professional nurse until the physician or professional nurse is of the opinion that the attendance of such persons is no longer necessary."

Volunteer ambulance personnel also expressed consternation at the Department of Health and Welfare's activities in the promulgation of licensing

standards for ambulance services and personnel. As a result, the Legislature took steps to insure proper public promulgation of proposed regulations and public hearings on such proposals. It also preempted the Department's ability to require successful completion of an emergency medical training course as a condition of licensure of volunteer ambulance personnel except under certain conditions, including a requirement that the State or local authorities pay two-thirds of the cost of such a course.

MEDICAL EDUCATION

While a proposal to authorize the University of Maine to develop a medical school failed as the result of a gubernatorial veto, the Legislature did take steps in the field of medical education by appropriating funds to provide tuition assistance to allopathic, osteopathic and dentistry students. It also enacted legislation proposed by Senator Gahagan of Caribou authorizing the Board of Registration in Medicine to utilize funds collected through licensure fees for the conduct of medical education programs and operation of a program of financial assistance "to medical students indicating an interest to engage in family practice in rural Maine. . . ."

GOOD SAMARITAN LAWS

As a result of initial proposals by Representatives Peter J. Curran of South Portland and Bonnie D. Post of Owls Head, the Judiciary Committee reviewed all the "good samaritan laws" on the books. Since these laws indicated that a person was not liable if they were in the exercise of due care and since persons are, as a matter of law, not negligent if in the exercise of due care, the committee determined that the existing laws were illusory in nature. Therefore, the committee reported out legislation repealing the various specific immunity provisions and replacing them with a law which grants immunity from civil liability to any person "who voluntarily, without the expectation of monetary or other compensation, renders first aid, emergency treatment or rescue assistance to a person who is unconscious, ill, injured or in need of rescue assistance. . . ." unless the rescuer is determined to have been willful, wanton, reckless or grossly negligent. Maine now has a Good Samaritan law!

HOSPITAL ADMINISTRATIVE DISTRICTS

During the session, the Legislature took action authorizing the establishment of a Hospital Administrative District in the Milo area at such time as the voters of the defined area approved a referendum. Modifications were made in the enabling legislation of HAD #1 and HAD #4 and authorization was granted permitting the dissolution of HAD #3 in Aroostook and Penobscot Counties.

CENTRAL LICENSING OF PROFESSIONALS

Responding to a gubernatorial request, the Legislature's Committee on State Government, chaired by Senator Theodore S. Curtis, Jr. of Orono and Representative Leighton Cooney of Sabattus, reported out legislation creating a "Central Professional and Occupational Licensing Bureau." The Bureau proposal had been opposed by the various professions as duplicative in nature and, therefore, an unnecessary expense. The Legislature did not, however, set forth the basis upon which the Bureau would operate and delegated to the State Government Committee the task of placing the flesh on the skeleton. The law directs the Committee to "prepare a plan of organization and operation for the bureau" and to present such a plan to the next special session.

ANATOMICAL GIFTS

Representative Anne M. Boudreau of Portland was successful in securing passage of legislation directing the Secretary of State to provide a form on each driver's license whereby an individual could make an anatomical gift. Certain clarifications were also made to the existing anatomical gift law.

CERTIFICATES OF NEED

The Health and Institutional Services Committee, looking toward future compliance of federal law, directed the State Department of Health and Welfare to begin the preparation of proposed Cer-

tificate of Need legislation for the 108th regular session in 1977. This legislative action specifically states that professional providers are to be involved in the process.

SUMMARY

Of the 733 public and private laws enacted by the 107th regular session, at least 10 percent dealt directly with some facet of the health care delivery system in Maine. Many more, of course, impacted upon the system on a general basis such as laws relating to employment practices, minimum wages, provisions of credit to patients, and the municipal payment of services provided to indigents. Many other legislative proposals dealing with health care issues did not win legislative approval this year. That does not mean that such issues have been dismissed. It merely means a postponement of further consideration until sometime in the future.

It is incumbent upon both professional providers of service and the consumer recipients of such services to provide information and input to the legislative process. This review indicates the complexity of the issues in the health care field with which 184 men and women and their staff are called upon to make decisions. All of these decisions were made within the scope of six calendar months and 109 actual legislative days. A clear understanding of the facts is the only basis upon which informed choices can be made.

Fall Meeting of the M.M.A. House of Delegates

Saturday, December 13, 1975

Mid-Maine Medical Center, Waterville, Maine

12:30 P.M. — Registration; 1:00 P.M. — Lunch; 2:00 P.M. — Meeting

10:00 A.M. — Meeting of the Executive Committee

Postage due is a postage don't.

Postage due is a thing of the past. From now on, if you send us claims without enough postage, they may never get to us. Instead, they may either be returned to you or sent to the dead letter office.

This could cause a significant number of lost claims and delays. The people most affected will be you and your patient. And if the two of you aren't happy, we're not either.

So please make sure your claims mail is going out with the correct postage. A postage meter scale can help. A legible return address on every envelope can help, too.

We process your claims as fast as we possibly can. It's unfortunate when we're all held up by some missing ten cent stamps.



Maine Blue Cross and Blue Shield
110 FREE STREET, PORTLAND, MAINE 04101

New Law Affects Every Physician

Sec. 1. 32 MRSA § 2806 is enacted to read.

§ 2806. Prescribing and dispensing of drugs.

Every written prescription issued by a physician, osteopath or dentist in this State shall contain in the lower right-hand corner of such prescription form a box at least ½ inch by ½ inch.

The following words shall appear to the left of this box: "Any drug which is the generic or chemical equivalent of the drug specified above in this prescription may be dispensed provided that the drug dispensed is listed in the current edition of either the National Formulary or the United States Pharmacopoeia and provided that no check mark (✓) has been handwritten in the box in the right-hand lower corner."

Any pharmacist receiving a prescription in which no check mark (✓) is found in the box provided is authorized to substitute a generic or chemically equivalent drug for the drug specified on the prescription, provided that the substituted drug is listed in the current edition of either the National Formulary or the United States Pharmacopoeia and that the price of the substituted drug does not exceed the price of the drug specified by the prescribing physician, osteopath or dentist.

Any pharmacist who substitutes a generic or chemically equivalent drug under the provisions of this section shall inform the person to whom the drug is dispensed of the substitution. Whenever any substitution is made under the provisions of this section, the pharmacist shall cause the name of the drug manufacturer or distributor to appear on the container label of the drug dispensed.

This section shall not apply to prescriptions ordered by physicians or osteopaths for patients in hospitals when such prescriptions are filled by a hospital pharmacy.

Sec. 2. Effective date. The effective date of this Act shall be January 1, 1976.

SAMPLE

SAMPLE

SAMPLE

PHYSICIAN'S NAME

B.N.D.D. #

CITY _____ STATE _____

NAME _____ DATE _____

ADDRESS _____

R_x

Any drug which is the generic or chemical equivalent of the drug specified above in this prescription may be dispensed provided that the drug dispensed is listed in the current edition of either the N.F. or the U.S.P. and provided that no check mark (✓) has been handwritten in the box in the right-hand lower corner.



_____ M.D.



Putting out the fires of arthritic pain

Rheumatoid arthritis can sometimes spread like wildfire, with joint after joint going up inflamed: "The usual onset is manifested by spotty joint involvement but an acute onset of symmetrical polyarthritis may be noted."^{*}

If aspirin fails, consider Butazolidin alka. Giving one capsule four times a day often provides prompt, pain-relieving, anti-inflammatory action to help restore joint mobility. The results you can get within a week can be maintained on as little as one or two capsules daily.

Serious side effects can occur. Select patients carefully (particularly the elderly) and follow them closely in line with the drug's precautions, warnings, contraindications and adverse reactions. For full details, please read the prescribing information. It's summarized on the back of this page.

Butazolidin[®] alka

Each capsule contains:
100 mg. phenylbutazone USP
100 mg. dried aluminum hydroxide gel USP
150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.

**Fire fighter
for arthritic
flare-ups.**

Butazolidin® alka

Each capsule contains:
100 mg. phenylbutazone USP
100 mg. dried aluminum hydroxide gel USP
150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.

Ragan, C.: The Clinical Picture of Rheumatoid Arthritis. in Arthritis, ed. 8, edited by J. L. Hollander and D. J. McCarty, Jr., Philadelphia: Lea & Febiger, 1972, chap. 21, p. 335

Geigy

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Substitute alka capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia), dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Rheumatoid arthritis, osteoarthritis, bursitis, acute gouty arthritis and rheumatoid spondylitis.

Contraindications: Children, 14 years or less, senile patients, history or symptoms of GI inflammation or ulceration including severe, recurrent or persistent dyspepsia, history or presence of drug allergy, blood dyscrasias, renal, hepatic or cardiac dysfunction, hypertension, thyroid disease, systemic edema, stomatitis and salivary gland enlargement due to the drug, polymyalgia rheumatica and temporal arteritis, patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpre-

dictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and GI tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions, complete physical examination including check of patient's weight, complete weekly (especially for the aging) or an every two week blood check, pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult GI bleeding with anemia, gastritis, epigastric pain, hematemesis, dys-

pepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult GI bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusion, states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, dizziness, vertigo, coma, hyperventilation, insomnia, ulcerative stomatitis, salivary gland enlargement.

(B)98-146-070-J (10/71)

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardley, New York 10502

BU 10259



Maine Blue Cross and Blue Shield News

LOCAL CONFIDENTIALITY POLICY USED NATIONALLY

Maine Blue Cross and Blue Shield instituted a policy on the confidentiality of records for its internal operations in September of 1973.

A summary of the policy appeared on page 257 of the October 1974 issue of *The Journal of the Maine Medical Association*, and both the policy and a video taped employee orientation on the subject were sent to the National Association of Blue Shield Plans (NABSP).

Just recently, NABSP published a policy on the confidentiality of records. Briefly, the National policy states:

PUBLIC ACCESS AND RELEASE OF DATA

"It should be recognized that a Blue Shield Plan is a third party to the patient-physician relationship. Since Blue Shield's file is a secondary or duplicate copy of the physician's primary record, there should be no need to inquire into Blue Shield's file. Patient inquiries, therefore, regarding medical data should be referred to the physician. However, Blue Shield may nonetheless become involved in a formal request. Therefore, the following guidelines should be applied:

1. In general, medical information should not be released without a court order.
2. Medical information should never be released over the telephone.
3. Medical information may be released in the aggregate form; however, requests for such data should be in writing and should include the purpose for which the data will be used.
4. Medical information may also be released to the extent necessary for appropriate peer review bodies to assist in claims determination relative to costs and quality of care.
 - a. In these situations, patient identification should be deleted."

INTERNAL ACCESS AND HANDLING OF MEDICAL INFORMATION

1. Access to medical information should be limited to a "need to know" basis.
2. Adequate orientation and training programs should be developed and maintained.
3. Plan employees should seek only that data necessary to adjudicate a claim, case or utilization patterns and profiles.
4. Adequate security precautions should be implemented to limit access to computers and data banks to those operating the systems.
5. Employees should be encouraged to handle confidential data in a professional manner.

"In addition to a review of existing safeguard procedures," states the Policy Letter, "Plans are encouraged to communicate their activities to their subscribers and physicians. It is essential that their understanding and cooperation be gained in order that any procedures implemented by the Plan may be effectively administered."

Maine Medical Association

SPECIAL COMMITTEES — 1975-1976

Special Committees for 1975-1976 as appointed by the President of the Maine Medical Association, Euclid M. Hanbury, Jr., M.D., Belfast.

Committee on Aging

James H. Bonney, M.D., 53 Chadwick St., Portland 04102 —
Chairman

Ad Hoc Committee on Alcoholism

Frank H. Lawrence, M.D., 22 Bramhall St., Portland 04102
Frederick S. Larned, M.D., 155 Spurwink Ave., Cape Elizabeth
04107

David W. Schall, M.D., 56 Baribeau Dr., Brunswick 04011
Winford Adams, M.D., 14 Starlight Dr., Brewer 04412
Irving I. Goodof, M.D., Thayer Hospital, Waterville 04901

Amy W. Pinkham Fund Committee

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Virginia C. Hamilton, M.D., South Harpswell 04079
Charles E. Burden, M.D., 1 North St., Bath 04530
Lloyd G. Davies, M.D., 249 Ocean House Rd., Cape Elizabeth
04107

Arthritis Committee

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Charles R. Glassmire, M.D., 37 Deering St., Portland 04101

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Paul Cummings, M.D., 10 High St., Lewiston 04240
Charles E. Dixon, M.D., 489 Essex St., Bangor 04401
Jean J. Labelle, M.D., 25 Bramhall St., Portland 04102

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Henry J. Wheelwright, M.D., Augusta Gen. Hospital, Augusta
04330

Richard T. Chamberlin, M.D., P.O. Box 706, 99 Western Ave.,
Augusta 04330

Advisers

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Miss Alice Russell, PTO, 92 Exchange St., Portland 04111

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ville 04901

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Euclid M. Hanbury, Jr., M.D., Medical Building, Belfast 04915

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Llewellyn W. Cooper, M.D., Hancock St., Bar Harbor 04609
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Eugene Beaupre, M.D., Thayer Hospital, Waterville 04901 (Nonmember of M.M.A.)

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John A. Root, M.D., 22 White St., Rockland 04841
Emerson H. Drake, M.D., 19 Bramhall St., Portland 04102
Richard C. Britton, M.D., Maine Medical Center, Portland 04102

Annual Meeting Dates For Your 1976 Calendar . . .

Maine Medical Association, June 5-8

Treadway-Samoset, Rockport

American Medical Association, June 26-July 1

Dallas

Letter to the Editor

To the Editor:

In recent communications to physicians, the Maine Department of Health and Welfare has passed along information about sources of antirabies serum and vaccine.

We have been contacted by the pharmacy at the Maine Medical Center giving the following additional in-state sources of these products.

This information is listed below simply for the information and convenience of physicians and their patients. The listing in no way implies endorsement of these firms by the Department of Health and Welfare.

This office will continue to distribute similar information,

through this publication and other sources, to physicians and other interested parties in Maine.

Human Rabies Immune Globulin: Maine Surgical Supply Co., 52 Marginal Way, Portland, Maine 04104 (207) 772-4601.

Antirabies Serum: Cook, Everett & Pennell, Riverside Industrial Park, Portland, Maine 04104 (207) 797-8330 and J. E. Goad & Co., Riverside Industrial Parkway, Portland, Maine 04104 (207) 797-2912.

Rabies Vaccine: Cook, Everett & Pennell, (Same as above) and J. E. Goad & Co., (Same as above).

PETER J. LEADLEY, M.D.
Director of Health

NEWS, NOTES AND ANNOUNCEMENTS - Continued from Page VI

are constantly being clarified and developed through research and clinical experience. An outstanding faculty of basic scientists and clinicians with special expertise in the investigation and treatment of depression will present current information on the nature and management of depressive disorders. The two-day conference will consist of formal didactic sessions and an informal evening session at which time conferees and faculty will be able to exchange information on their interests and professional experiences with varied aspects of psychiatric depression.

Program Director: William E. Fann, M.D.

Accreditation

This Continuing Medical Education offering meets the criteria for 15½ hours of credit in Category 1 for the Physician's Recognition Award of the American Medical Association, and is acceptable for 15½ Prescribed hours by the American Academy of Family Physicians.

For further information contact The Office of Continuing Education, Baylor College of Medicine, Texas Medical Center, Houston, Texas 77025 (713) 790-4941.

Mid-Winter Virgin Islands Clinical Conference

This Mid-Winter Virgin Islands Clinical Conference will be held in St. Thomas, January 29, 30, 31, 1976 by the U.S. Virgin Islands Medical Society in association with The Faculty of the University of Pennsylvania School of Medicine.

This program is acceptable for 14 credit hours in Category 1 for the Physician's Recognition Award of the A.M.A., and will include lectures and seminars of interest to the physician in General Practice, Internal Medicine, General Surgery and OB-Gyn.

For further information, write AIRMAIL to: Harold A. Hanno, M.D., F.A.C.P., Secretary, U.S. Virgin Islands Medical Society, Box 1442, St. Thomas, Virgin Islands 00801.

Postgraduate Seminar in Emergency Medicine

ADVANCED LIFE SUPPORT: THE FOURTH ANNUAL POSTGRADUATE SEMINAR IN EMERGENCY MEDICINE; March 19-22, 1976; Americana Hotel, Miami Beach, Florida.

Sponsored by the Florida Chapters of the American College of Emergency Physicians and the Emergency Department Nurses Association.

Fees: \$125 (ACEP), \$150 (Non-ACEP Physician), \$75 (EDNA), \$100 (Non-EDNA Nurse), \$75 (Registered EMT - State or National), \$100 (Non-Registered EMT), \$40 (Interns and Residents with letter from Department Head), \$100 (Administrators, Planners, and Others).

For further information contact: Registrar, 1976 PGS, 1919 Beachway Road, Suite 5-C, Jacksonville, Florida 32207 (904) 399-0510.

Course in Clinical Neuro-Otolaryngology

The University of Pittsburgh School of Medicine announces the Third Course in Clinical Neuro-Otolaryngology will be held on March 25, 26 and 27, 1976 at the Eye and Ear Hospital of Pittsburgh. This course is designed for the practitioner of Otorhinolaryngology or Neurology and residents in training, to aid in the understanding of the various neurological aspects of otorhinolaryngological disorders. The focus will be on practical clinical evaluation and management.

Topics covered will include the function, clinical evaluation, and disorders of the vestibular system, audition, taste, olfaction, speech, swallowing, and the facial nerve. There will be brief formal presentations. However, the emphasis will be on panel conference-type discussions, with case presentations, to encourage the active discussion and participation of the faculty and the participants. The course is acceptable for AMA credit hours in Category 1.

Sponsored by the Department of Otolaryngology and the Division of Continuing Education, University of Pittsburgh, School of Medicine.

For further information, please write to: Sidney N. Busis, M.D., Course Director, Eye and Ear Hospital of Pittsburgh, Pittsburgh, Pennsylvania 15213.

Emergency Division Physician

Emergency physician to practice and teach 42 hours/week in 563 bed hospital beginning December 15, 1975; 50,000 cases/year; departmental status; university affiliation, 72 house staff; salary \$32,500/year with standard fringes.

Contact: F. Lawrence, M.D., Director, Department of Emergency Medicine, Maine Medical Center, Portland, Maine 04102.

County Society Notes

Washington

The regular meeting of the Washington County Medical Society was held on Monday, April 28, 1975 at the Staff Lounge, Down East Community Hospital, Machias, Maine with seven members and guests present.

Discussion of correspondence from the Maine Medical Association in regards to increasing the dues. Considerable discussion but no definitive action taken, but general feeling that there should be no great increase in annual dues. Discussion also in changes in Bylaws. Discussion of Sen-Cit, Eastern Task Force on Aging on their Health Screening; also a discussion on the Children & Youth Program for Washington County, Maine with no particular action taken.

KARL V. LARSON, M.D., *Secretary*

Lincoln-Sagadahoc

The regular monthly meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges Inn, Wiscasset on May 20, 1975, with thirty-seven members and guests present.

The business meeting was called to order at 8:45 p.m. by the President, Dr. Ralph C. Powell. The minutes of the April meeting were accepted as read.

There was no old business.

The application for membership of Dr. Herbert M. Baganz, Jr. was read and recommended by the Board of Censors. The application was unanimously approved.

The secretary read a letter from the Androscoggin County Medical Society describing certain dissatisfaction with Maine Blue Cross and Blue Shield; discussion followed.

Dr. Richard C. Leck described actions taken in the State of New York to change the professional liability situation.

Dr. Robert H. Dixon introduced Dr. Alex J. Norzow, who described his recent trip to Russia and spoke on Russian medicine.

The regular September meeting of the Lincoln-Sagadahoc County Medical Society was held at The Ledges in Wiscasset, Maine on Tuesday evening, the 16th.

There were twenty-five members and guest present for the dinner and meeting.

The meeting was called to order at 8:21 p.m. by the President, Dr. Ralph C. Powell; the minutes of the May meeting were read by the Secretary and accepted as read.

Dr. Powell introduced Dr. Paul H. Dumdy, who presented Mr. Robert Gordon, of the Merrymeeting Alcoholic Treatment Center, in Bowdoinham; Mr. Gordon described the program at Merrymeeting House, and he and Dr. Aldo F. Llorente answered many questions.

There was no old business. New business was introduced by Dr. Powell. He read a request from Mrs. Shirley Smith that the County Society Medical Auxiliary have dinner with the Society every other month and have a separate meeting afterward. Dr. David W. Schall moved that physicians invite their wives to dinner every other month. The motion was seconded and passed. Dr. Powell then read a letter from Dr. Bates, in Eastport, advising that that town would welcome the relocation of a physician to it.

Dr. Robert M. Hassan discussed the Diabetic Detection Drive to be held in November throughout the State.

Dr. Anthony J. Horstman, Delegate, reported that Dr. Richard C. Leck is the President-elect of the M.M.A., that dues will rise to two hundred dollars a year next year, plus a possible assessment of up to one hundred dollars for a new M.M.A. office. Dr. Leck described efforts so far to find an Assistant Executive Director.

The meeting was adjourned at 9:15 p.m.

GEORGE W. BOSTWICK, M.D., *Secretary*

Oxford

The annual spring meeting of the Oxford County Medical Society convened at the Bethel Inn at 5:30 p.m.

There were fourteen members attending and three guests.

The meeting was called to order by the President, Dr. Stephen B. Dewing, who introduced the speaker, James F. McMichael, President of Union Mutual Management Corporation, who gave an interesting and well-delivered talk on managing money and his company's concept of Individual Asset Management.

The business meeting was then begun and the minutes of the fall meeting were read and accepted.

Old business: It was reported that Drs. Ann S. Bonhaus, Robert S. Bausch and Jerome Dunst had been accepted into membership through individual meetings in Rumford and Norway since the last meeting.

New business: A nominating committee was appointed by the President, Dr. Stephen Dewing to consist of Drs. Linwood M. Rowe, Eugene Gorayeb, Harry L. Harper and Kenneth G. Hamilton. Letter to the Society was read by President Dewing from Dr. Fishman, President of the Androscoggin County Medical Association, urging our support for their resolution calling for a communication of urgency with respect to the malpractice crisis. It was moved, seconded and passed that we support this resolution unanimously. Dr. Albert P. Royal, Jr. brought to our attention that a sequence of unplanned events had made the county's only delegate now the secretary and potentially destroyed one of the county's votes in the House of Delegates. It was suggested that if the alternate is not going to be able to attend the up-coming meeting, to have an alternate-alternate appointed and empowered to vote as a delegate. This will be done. Dr. James A. Edmond pointed out that there was some apparent sentiment noted at a recent Continuing Education Committee Meeting of the M.M.A. suggesting that perhaps a full-time Executive Director might be more helpful than securing an assistant to the current Executive Director. This was discussed. Motion was made, seconded and passed instructing the delegates to support any activity in this direction if they surface at the up-coming meeting of the House of Delegates.

It was pointed out by Dr. Harper that some new members in the Norway area had not yet been added to the rolls of the M.M.A. and received their mailings. The secretary apologized for this and assured membership that he would take care of the matter.

Our guest, Dr. H. Carl Amrein from the Executive Council answered a few questions and made some comments to points of interest from the Executive Council level.

Dr. Walter G. Dixon introduced his guest, Dr. Victor M. Parisien of Lewiston, who is also actively involved in orthopedics at the Stephens Memorial Hospital.

After deciding to hold the next meeting in October, at a time and place to be decided, the membership adjourned to dinner.

DAVID L. PHILLIPS, M.D., *Secretary*

Cumberland

The Executive Committee of the Cumberland County Medical Society met at the Mercy Hospital in Portland, Maine on July 8, 1975.

Members present: Drs. Robert E. McAfee, President; Wesley J. English, Secretary-Treasurer; Walter B. Goldfarb, Vice-President; Harry A. Bliss and Douglas R. Hill. Guest present: Dr. Stuart W. McGuire.

1. As noted above, all members present except Dr. Ronald J. Carroll.

2. Dr. McGuire reported arrangements being finalized for annual outing on Thursday, September 18, 1975 at the Homewood Inn. Cost includes \$125.00 for use of the premises. There will be a cash bar, and there will be a choice of lobster or

steak. Beer will cost \$16.00 a case.

3. Report of the Maine Medical Association Meeting in Rockport, Maine June 14-15, 1975 — Dr. Douglas R. Hill:

- A. Each county should appoint a Legislative Action Committee.
 - B. Each county should appoint a Mental Health Committee.
 - C. Report on Pineland Hospital — Mental Health Committee charged with responsibility to visit Pineland and make report.
 - D. Progress on new Assistant Executive Director. County dues increased to \$200.00 per year to support an Assistant Executive Director. Dr. Hanley and Dr. Leck to interview candidates. Space is a problem since there is no further room in the Bowdoin infirmary to expand.
 - E. Malpractice — Dr. Kittredge our State representative to a national conference.
 - F. Next year there will be more emphasis on educational courses for doctors at the annual meeting.
4. Malpractice — Report by Dr. McAfee:
- A. The insurance commissioner of the State of Maine authorized to organize a joint underwriting commission to provide insurance to those with no insurance.
 - B. Blue Ribbon Commission appointed to suggest changes in malpractice procedure (changes we would like to see involve: 1) change in the statute of limitations, 2) a sliding contingency fee scale, 3) limit of liability to \$100,000, and 4) reporting of all successful suits to the Board of Registration in Medicine). This Commission will not be meeting before October of 1975.
 - C. The AMA is to form a Reinsurance Company to supply umbrella coverage.
5. Report of the AMA — Dr. McAfee:
- A. Dues are going up.
 - B. A lot more aggressiveness noted in the meeting of the House of Representatives.
 - C. Elections — The new president is to be Dr. Sodeman, a pathologist.
 - D. Dr. McAfee described the official policy on strikes.
 - E. The Fall meeting will be held in Honolulu.
6. A letter was received from Dr. A. Dewey Richards, requesting transfer of his membership from the Cumberland County Medical Society to Penobscot County Medical Society.
7. Report on Primary Care Facility — Dr. Bliss:
- A. A Board of Corporators has been formed.
 - B. Estimates of cost have been made.
 - C. An endorsement needed from the Cumberland County Medical Society. (This endorsement is provided by letter and authorized by the Executive Committee this date).
8. Unfinished business — Resolution on death of Dr. Douchinett tabled. To be read at October meeting.
9. The meeting adjourned at approximately 8:00 p.m.

WESLEY J. ENGLISH, M.D., *Secretary-Treasurer*

Kennebec

The Council of the Kennebec County Medical Association met at The Holiday Inn in Augusta, Maine at 7:00 p.m. on September 11, 1975. In attendance were the President, Dr. Joseph J. Hiebel, the Vice-President, Dr. James C. Hayes; the Secretary, Dr. Oscar T. Feagin; Councillors, Dr. Richard E. Barron and Dr. Valentine J. Moore; and member of the Executive Committee of the Maine Medical Association, Dr. Richard T. Chamberlin.

The first portion of the meeting was given over to relatively routine business. The applications of Dr. Nancy Coyne and Dr. Robert Day were approved. The transfer of Dr. Daniel Storer to the Kennebec County Medical Association was approved. Resignations of Drs. Ralph G. Bennett, Jr. and James C. Wren were accepted. A communication from Mrs. Bergeron of the Maine Medical Association concerning delayed payment of dues by Dr.

James Butler was read. It was decided that the bylaws state that full membership is completed upon payment of dues. Dr. Butler did not request affiliate membership for any particular reason, and it was the consensus of the Council, since he had not paid his dues, he was not a full member at this time. He is to be informed of this fact.

Several communications were read and discussed. First, was a letter from a Citizens Commission on Human Rights offering amnesty to members of the Association who agree to confess to crimes against mental patients. This is to be filed. Dr. John Reynolds notified the Association of the death of his father, Dr. Ralph Reynolds. Dr. Hiebel is to arrange for a memorial resolution. Correspondence between Dr. Hiebel, Dr. Hanbury and Dr. Ordway regarding Mental Health Committees was read. It was felt that as the Kennebec County Medical Association includes the staff members of the Augusta Mental Health Institute, the County Association as such does not need to have any Mental Health Committee. A letter from a patient in Randolph registering a complaint about one of our members was read. It was felt by the Council that he did not act on an unethical or unprofessional fashion, and that the major problem was a communication failure. No action is to be taken. A letter from the American Medical Association in regard to dues structure was read. A letter from the Secretary of HEW designating the Pine Tree Organization as a PSRO agency for the State was read and filed.

New Business: Dr. Feagin raised a question of a letter to the complaint column of the Kennebec Journal about physicians' fees and asked whether the County Association should respond to such letters in any way. A vigorous discussion of the public relations of the medical profession with the public, was then held. It was decided that the County Association might explore with some public relations expert whether or not a public relations campaign was in order to attempt to inform the members of the public about the nature of physicians' fees, services, tasks and obligations. Dr. Feagin volunteered to write a response to the KJ about the letter that was in the paper.

Dr. Hiebel stated his intention to appoint Dr. Joseph Crawford of Augusta as a Kennebec Council Society Member of the Insurance Committee of the Maine Medical Association. Considerable discussion was devoted to the matter of the bylaws which have been hanging fire since 1973. The changes in the bylaws were presented to the Council and a difficulty with disciplinary procedures still exist. Dr. Chamberlin states that he would check with Dr. Hanley as to what happened about this matter, and it was surmised that there was a legal opinion about the nature of the disciplinary procedures.

Finally, the Fall programs were discussed. Several possible programs were mentioned and Dr. Feagin will arrange for them. Dr. Chamberlin presented the recent deliberations of the Executive Committee of the Maine Medical Association. He mentioned nine items which were of current importance: 1) The question of improving communication between the profession and the legislature and how to inform the physicians what was happening in the State House, 2) Dr. Hanley's recommendations to physicians as to what procedure to follow if an insurance company threatened to drop a physician's malpractice coverage, 3) The State Malpractice Commission. Dr. Chamberlin stated that Dr. Kittredge and Dr. Reynolds had been appointed to this Commission, 4) Changes in the budget and dues of the Maine Medical Association, 5) The question of an assistant to Dr. Hanley, 6) The current status of Health Manpower Bill, 7) The current status of the Health Services Agency situation, 8) The recent court decision which puts in serious doubt the legality of one man corporations, and 9) The fact that the Executive Committee had reaffirmed its support of the Medical School and what the recently formed Commission was up to. The Council adjourned at approximately 10:30 p.m., in preparation for the full meeting of the Association the following week.

OSCAR T. FEAGIN, M.D., *Secretary*

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

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surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of child-bearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies.

Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle

spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



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Left Ventricular Aneurysm in a Patient With Normal Coronary Arteries and No History of Myocardial Infarction

JOE R. WISE, JR., M.D. and JAMES K. CONRAD, M.D.

ABSTRACT

A 36-year-old man with recurrent systemic emboli and no history of myocardial infarction was found to have clinical signs of left ventricular aneurysm. Cardiac catheterization revealed normal coronary arteries and a large dyskinetic area of the anterior and apical portion of the left ventricle.

Aneurysm of the left ventricle is usually the result of transmural myocardial infarction and is almost invariably associated with demonstrable coronary artery disease.¹ Other less frequent causes of left ventricular aneurysm include sarcoidosis,² syphilis,³ fungus disease,³ rheumatic fever,³ chest trauma,⁴ Chagas disease,⁵ congenital defects.⁶⁻¹⁰ The purpose of this report is to describe the occurrence of a left ventricular aneurysm in a 36-year-old man with normal coronary arteriograms and no history of myocardial infarction. The etiology of this aneurysm remains undetermined.

CASE REPORT

N.C., a thirty-one-year-old man, was well and active until 1971 when he developed claudication, and subsequently gangrenous skin changes over the dorsum of the right foot and toes. Arteriogram showed occlusion of the femoral artery on the right at the level of Hunter's canal and occlusion of the popliteal artery on the left. A diagnosis of Burger's disease was made and right lumbar sympathectomy was performed. The skin lesions healed but stable claudication persisted in the right leg. In June 1974, he was hospitalized at the Eastern Maine Medical Center following a sudden episode of confusion and aphasia. He denied

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cardiovascular symptoms. His blood pressure had been normal and there was no family history of cardiovascular disease. Prior to 1971, he smoked cigarettes.

At the time of admission, the blood pressure was 140/80. He was moderately obese. The jugular venous pressure was not raised and the carotid pulsations were normal. The chest was clear. The left ventricular impulse was abnormally sustained and displaced laterally. The first and second heart sounds were normal, a third heart sound was present and no murmurs were heard. The femoral pulses were present but decreased on the right. No pulses were palpable in the right foot. There was a faint posterior tibial pulse on the left. No ischemic skin changes were noted. Neurologic examination was within normal limits except for mild aphasia and confusion which spontaneously improved during his hospital stay. Complete blood count, urinalysis, blood urea nitrogen, cholesterol, triglyceride and blood sugar were all normal. Brain scan revealed an area of abnormally increased uptake on the left occipital region and cerebral arteriogram showed elevation of the posterior branches of the middle cerebral artery. Other studies included a negative LE prep, sedimentation rate of 5 and normal serum electrophoresis. Cryoglobulins and macroglobulins were not present. The chest x-ray showed normal heart size and clear lungs. The electrocardiogram showed a qR in leads II, III, AVF and V-4 through V-6 and was similar to the tracing of 1971 (Fig. 1). The echocardiogram did not show any evidence of atrial myxoma. Cardiac catheterization on 8/6/74 showed normal coronary arteries (Fig. 2). The left ventricular end diastolic pressure was 15 mm Hg, and there was an extensive area of dyskinesis involving the anterior left ventricular apex (Fig. 3). No mitral regurgitation was seen. The ejection fraction was 50%. Oral anticoagulants were begun and he was discharged to be followed as an out-patient.

DISCUSSION

A variety of syndromes previously attributed to coronary artery disease have been described in patients with angiographically normal coronary artery anatomy. An increasingly large group of patients

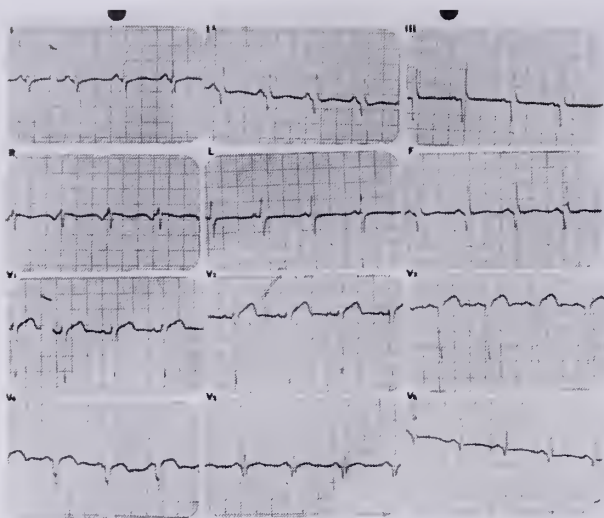


Fig. 1. Electrocardiogram June 1974 showing Q waves in the inferior and lateral leads.

with clinically typical angina pectoris have been found to have normal coronary arteriograms.¹¹⁻²¹ A few patients with normal arteriograms have had myocardial infarction²²⁻²⁹ and in some post-mortem examination has not shown any coronary artery disease.^{28,30}

Several explanations have been offered for these apparently contradictory occurrences. Ensente reported apparent regression of coronary artery disease in two patients studied with serial coronary arteriography over a period of one year and suggests that hemorrhage into an arteriosclerotic plaque with subsequent partial resolution might account for the findings in these patients.³¹

Coronary artery spasm, long suspected as a cause for myocardial ischemia, has been demonstrated angiographically in some patients with angina pectoris.³²⁻³⁴ This spasm is thought to be transient; however, Cheng described an instance of acute myocardial infarction which apparently resulted from coronary artery spasm occurring at the time of coronary arteriography.²⁷

Obstruction of a coronary artery due to thrombosis or embolism with subsequent lysis could explain the occurrence of myocardial infarction in patients with a normal coronary arteriogram.³⁵ Brauschke described one patient followed with serial arteriograms who apparently recanalized an obstructed vessel following myocardial infarction.³⁶

Disease of vessels too small to be demonstrated angiographically may cause myocardial damage in some patients with apparently normal coronary arteries.³⁷⁻³⁸ Arteriolar abnormalities have been found in biopsy specimens taken from the right ventricular apex and septum in a small group of patients with clinical evidence of coronary artery disease and normal arteriograms.³⁷ Areas of myocardial

scarring and degeneration have been seen in association with small vessel disease,³⁸ but it seems unlikely that occlusion of small vessels would result in focal transmural myocardial infarction and aneurysm formation and there are no reports of this type in the literature.

In some patients myocardial ischemia and necrosis in the presence of normal coronary arteries has been associated with abnormalities of hemoglobin-oxygen dissociation,¹⁵ but this has been an infrequent finding and the significance of this association is not clear.³⁹ Congenital aneurysms of the left ventricle have been described. Most of these patients have been Negroes and most aneurysms have been found in the subvalar region of the left ventricle though apical aneurysms have been reported.¹⁰

Segmental areas of left ventricular dysfunction have been described in patients with transmural myocardial infarction and normal coronary arteries and, though unusual, ventricular aneurysm has been reported in these circumstances.^{29,31,36,41,42} One of Esente's patients with ventricular aneurysm and normal coronary arteries did not have a history of myocardial infarction and in that respect resembles the patient described here. Maloy described a young woman with a large apical aneurysm who had recurrent ventricular arrhythmias and episodes of chest pain. No myocardial infarction was documented and at autopsy the coronary arteries were normal.⁴⁰

Although regional left ventricular wall abnormalities are usually considered to be a sign of ischemic heart disease, abnormal left ventricular contraction patterns have been described in patients with primary myocardial disease. Kreulen, et al studied 34 patients with cardiomyopathy and were able to divide these patients into three groups based on their left ventriculogram.⁴³ Ten patients (group III-B) had segmental areas of asynergy similar in appearance and distribution to those found in patients with coronary artery disease. These authors suggested that coronary artery emboli or endomyocardial fibrosis might be responsible for these localized areas of left ventricular dysfunction in these patients with what is assumed to be a diffuse myocardial process. The segmental left ventricular contraction abnormalities found in some patients with mitral valve prolapse, often associated with ventricular arrhythmias and left ventricular hypertrophy, may be due to some form of cardiomyopathy.⁴⁴

Which of these factors was responsible for the aneurysm in the patient described above is not known. The aneurysm may be a congenital muscular defect or, less likely, the result of small vessel disease. An alternate explanation is that the aneurysm in this case is the result of some form of cardiomyopathy. Although areas of dyskinesia or

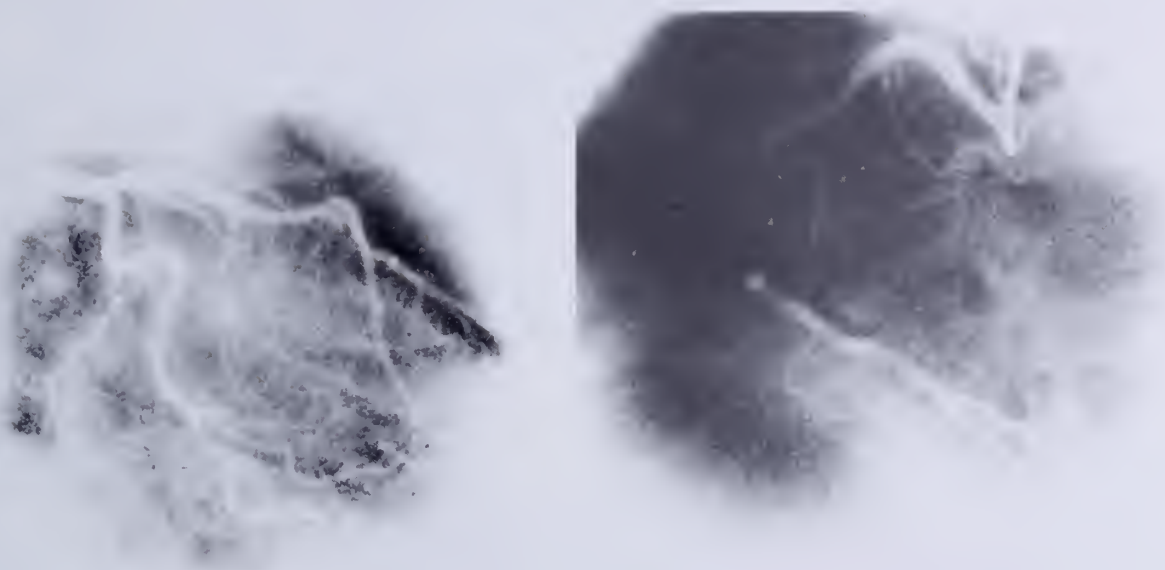


Fig. 2. Selective coronary arteriograms showing normal left and right coronary arteries.



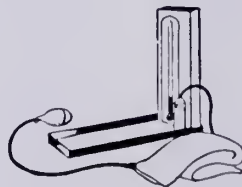
Fig. 3. End-diastolic and end-systolic frames of the left ventricular cine-angiogram showing a large left ventricular aneurysm. The filling defects most apparent in the end-systolic frame may represent mural thrombus.

aneurysm are not usually seen in patients with cardiomyopathy, it may be that a non-contractile, myopathic segment might become aneurysmally dilated such as areas of infarcted myocardium appear to do.

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Precautions: Do periodic serum electrolyte and

BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Anti-hypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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Contraindicated in CNS depression from drugs; in the presence of evidence of bone marrow depression; and in patients hypersensitive to phenothiazines or amitriptyline. Should not be used during the acute recovery phase following myocardial infarction or in patients who have received an MAOI within two weeks. Patients with cardiovascular disorders should be watched closely. Not recommended in children or during pregnancy. The drug may impair mental or physical abilities required in the performance of hazardous tasks and may enhance the response to alcohol. Antiemetic effect may obscure toxicity due to other drugs or mask other disorders. Since suicide is a possibility in any depressive illness, patients should not have access to large quantities of the drug. Hospitalize as soon as possible any patient suspected of having taken an overdose.

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WARNINGS: TRIAVIL should not be given with guanethidine or similarly acting compounds. Use cautiously in patients with history of urinary retention, angle-closure glaucoma, increased intraocular pressure, or convulsive disorders. In patients with angle-closure glaucoma, even average doses may precipitate an attack. Patients with cardiovascular disorders should be watched closely. Tricyclic antidepressants, including amitriptyline HCl, particularly in high doses, have been reported to produce arrhythmias, sinus tachycardia, and prolongation of conduction time. Myocardial infarction and stroke have been reported with tricyclic antidepressant drugs. Close supervision is required for hyperthyroid patients or those receiving thyroid medication. Caution patients performing hazardous tasks, such as operating machinery or driving motor vehicles, that drug may impair mental and/or physical abilities. Not recommended in children or during pregnancy.

PRECAUTIONS: Suicide is a possibility in depressed patients and may remain until significant remission occurs. Such patients should not have access to large quantities of this drug.

Perphenazine: Should not be used indiscriminately. Use with caution in patients who have previously exhibited severe adverse reactions to other phenothiazines. Likelihood of untoward actions is greater with high doses. Closely supervise with any dosage. The antiemetic effect of perphenazine may obscure signs of toxicity due to overdosage of other drugs or make more difficult the diagnosis of disorders such as brain tumor or intestinal obstruction. A significant, not otherwise explained, rise in body temperature may suggest individual intolerance to perphenazine, in which case discontinue.

If hypotension develops, epinephrine should not be employed, as its action is blocked and partially reversed by perphenazine. Phenothiazines may potentiate the action of central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol) and atropine. In concurrent therapy with any of these, TRIAVIL should be given in reduced dosage. May also potentiate the action of heat and phosphorus insecticides.

Amitriptyline: In manic-depressive psychosis, depressed patients may experience a shift toward the manic phase if they are treated with an antidepressant. Patients with paranoid symptomatology may have an exaggeration of such symptoms. The tranquilizing effect of TRIAVIL seems to reduce the likelihood of this effect. When amitriptyline HCl is given with anticholinergic agents or sympathomimetic drugs, including epinephrine combined with local anesthetics, close supervision and careful adjustment of dosages are required.

Caution is advised if patients receive large doses of ethchlorvynol concurrently. Transient delirium has been reported in patients who were treated with 1 g of ethchlorvynol and 75-150 mg of amitriptyline HCl.

Amitriptyline HCl may enhance the response to alcohol and the effects of barbiturates and other CNS depressants.

Concurrent administration of amitriptyline HCl and electroshock therapy may increase the hazards associated with such therapy.

Such treatment should be limited to patients for whom it is essential. Discontinue several days before elective surgery if possible. Elevation and lowering of blood sugar levels have both been reported.

ADVERSE REACTIONS: Similar to those reported with either constituent alone.

Perphenazine: Side effects may be any of those reported with phenothiazine drugs: extrapyramidal symptoms (opisthotonus, oculogyric crisis, hyperreflexia, dystonia, akathisia, acute dyskinesia, ataxia, parkinsonism) can usually be controlled by the concomitant use of effective antiparkinsonian drugs and/or by reduction in dosage, but sometimes persist after discontinuation of the phenothiazine.

Tardive dyskinesia may appear in some patients on long-term therapy or may occur after drug therapy with phenothiazines and related agents has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. Symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth, or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Involuntary movements of the extremities sometimes occur. There is no known treatment for tardive dyskinesia; antiparkinsonism agents usually do not alleviate the symptoms. It is advised that all antipsychotic agents be discontinued if the above symptoms appear. If treatment is reinstituted, or dosage of the particular drug increased, or another drug substituted, the syndrome may be masked. It has been suggested that fine vermicular movements of the tongue may be an early sign of the syndrome, and that the full-blown syndrome may not develop if medication is stopped when lingual vermiculation appears.

Other side effects are skin disorders (photosensitivity, itching, erythema, urticaria, eczema, up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions); peripheral edema; reversed epinephrine effect; hyperglycemia; endocrine disturbances (lactation, galactorrhea, gynecomastia, disturbances of menstrual cycle); altered cerebrospinal fluid proteins; paradoxical excitement; hypertension, hypotension, tachycardia, and ECG abnormalities (quinidine-like effect); reactivation of psychotic processes; catatonic-like states; autonomic reactions, such as dry mouth or salivation, headache, anorexia, nausea, vomiting, constipation, obstipation, urinary frequency or incontinence, blurred vision, nasal congestion, and a change in pulse rate; hypnotic effects; pigmentary retinopathy; corneal and lenticular pigmentation; occasional lassitude, muscle weakness, mild insomnia. Other adverse reactions reported with various phenothiazine compounds include blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia); liver damage (jaundice, biliary stasis); grand mal convulsions; cerebral edema; polyphagia; photophobia; skin pigmentation; and failure of ejaculation.

Amitriptyline: Note: Listing includes a few reactions not reported for this drug, but which have occurred with other pharmacologically similar tricyclic antidepressant drugs. **Cardiovascular:** Hypotension; hypertension; tachycardia; palpitation; myocardial infarction; arrhythmias; heart block; stroke. **CNS and Neuromuscular:** Confusional states; disturbed concentration; disorientation; delusions; hallucinations; excitement; anxiety; restlessness; insomnia; nightmares; numbness, tingling, and paresthesias of the extremities; peripheral neuropathy; incoordination; ataxia; tremors; seizures; alteration in EEG patterns; extrapyramidal symptoms; tinnitus; syndrome of inappropriate ADH (antidiuretic hormone) secretion. **Anticholinergic:** Dry mouth; blurred vision; disturbance of accommodation; constipation; paralytic ileus; urinary retention; dilatation of urinary tract. **Allergic:** Skin rash; urticaria; photosensitization; edema of face and tongue. **Hematologic:** Bone marrow depression including agranulocytosis; leukopenia; eosinophilia; purpura; thrombocytopenia. **Gastrointestinal:** Nausea; epigastric distress; vomiting; anorexia; stomatitis; peculiar taste; diarrhea; parotid swelling; black tongue. **Endocrine:** Testicular swelling and gynecomastia in the male; breast enlargement and galactorrhea in the female; increased or decreased libido; elevated or lowered blood sugar levels. **Other:** Dizziness; weakness; fatigue; headache; weight gain or loss; increased perspiration; urinary frequency; mydriasis; drowsiness; jaundice; alopecia. **Withdrawal Symptoms:** Abrupt cessation after prolonged administration may produce nausea, headache, and malaise. These are not indicative of addiction.

OVERDOSAGE: All patients suspected of having taken an overdosage should be admitted to a hospital as soon as possible. Treatment is symptomatic and supportive. However, the intravenous administration of 1-3 mg of physostigmine salicylate is reported to reverse the symptoms of tricyclic antidepressant poisoning. Because physostigmine is rapidly metabolized, the dosage of physostigmine should be repeated as required particularly if life-threatening signs such as arrhythmias, convulsions, and deep coma recur or persist after the initial dosage of physostigmine. On this basis, in severe overdosage with perphenazine-amitriptyline combinations, symptomatic treatment of central anticholinergic effects with physostigmine salicylate should be considered.

For more detailed information, consult your MSD Representative or see full Prescribing Information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa 19486

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Dysmenorrhea, Acne and Painful Fingers

MASON TROWBRIDGE, JR., M.D.*

The triad of dysmenorrhea, acne, and painful fingers during the menses was reported by Dr. C. H. Lawrence† at a meeting of the Penobscot County (Maine) Medical Society on December 17, 1940. This author has seen two cases.

CASE REPORTS

Case #1: In the mid-forties, a young Air Force WAC reported to sick call at the Sioux Falls, S.D., air base. Her chief complaint was dysmenorrhea, and she obviously had acne. She almost burst out crying when the first question of the doctor was about tender fingers. All the physicians she had seen previously were frankly incredulous about her story and had no therapy to recommend. During the menses, her fingers looked as if they all had bilateral incipient paronychia. The lateral nail folds were chiefly involved. The fingers, as well as the acne and dysmenorrhea, responded in a gratifying manner to diethylstilbestrol.

Case #2: A nineteen-year-old spinster, studying piano at a conservatory of music, was seen in March 1970. Her periods were initially regular and very painful, acne became worse with her periods, and before her periods she felt as she were "developing hangnails." The most striking physical finding during her

periods was swelling, redness, and tenderness of the proximal folds of the nails (eponychiae). She responded well initially to 1.25 mg. conjugated estrogens (equine) (Premarin®) daily for three out of four weeks. When later taken off estrogen by another physician and given an oral contraceptive agent, the symptoms recurred. Also, after that, the fingers sometimes bled at the time of the menses in spite of the estrogen. But they were better, and the acne and dysmenorrhea were controlled. A letter from the patient in May 1975, stated, "Every year when I go for a physical, the doctors don't believe what I tell them . . . One advised me to go off the pill (estrogen) for the summer . . . I went off in April, and within six days my fingers began to bleed and my face became very oily. During the period that followed I had very bad cramps."

DISCUSSION

Lawrence has written on dysmenorrhea and acne, but no mention was found of painful or bleeding fingers. Efforts to find his colleagues have not been fruitful. Countless physicians, including dermatologists and gynecologists, have not heard of this syndrome. Correspondence with recognized authorities in female endocrinology and authors of monographs on the nails has been unrewarding.

Dr. Lawrence stated that it was handy to have a patient with acne, for its improvement indicated the appropriate dose of estrogen.

SUMMARY

Young women with dysmenorrhea, acne, and painful or bleeding fingers during the menses may be greatly improved by estrogen administration.

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†Former Chief of the Endocrine Clinic of the Boston Dispensary, New England Medical Center, Tufts Medical School, Boston, MA.

Reminder to M.M.A. Members

CONTINUING MEDICAL EDUCATION ACTIVITY REPORT

The bylaws of the Maine Medical Association were amended in June of 1973 as follows: Chapter I, Section 11, — "Each member of the Maine Medical Association shall be required to report his activities in continuing medical education every year according to a format provided by the Committee on Continuing Medical Education."

Only active, dues-paying members are required to report this year.

Please fill in your activity report promptly and return to the M.M.A. office, P.O. Box 250, Brunswick, Maine 04011.

Resolution of Complete Trifascicular Block

CAROLYN LINNEBUR, M.D.* and JAMES K. CONRAD, M.D.**

ABSTRACT

A 27-year-old woman, three months pregnant, developed syncopal episodes and was found to have complete A-V block due to trifascicular disease requiring pacemaker implantation. Over a period of 4 months, the conduction defects resolved leaving an electrical axis of -40 degrees as the only EKG abnormality. She has remained asymptomatic for 3 and one-half years and without pacemaker support for the past 3 years.

Trifascicular disease, once fully established, is usually permanent, and spontaneous resolution over this period of time has not before been reported.

Although intermittent conduction is commonly observed in the development of non-surgical tri-

fascicular block,¹ long term resolution of established heart block of this type has not to our knowledge been previously reported. In this presentation, we describe a patient with spontaneous remission of trifascicular block whose only residual electrocardiographic abnormality is slight left axis deviation. She has remained asymptomatic without EKG change for 32 months.

CASE REPORT

A 27-year-old woman, three months pregnant, was admitted to Bataan Memorial Hospital in March 1972 with a history of episodic dizziness and syncope of one month's duration. There was no prior history of cardiac disease, seizure activity, recent or remote infectious processes or other systemic illness. No members of the immediate family had syncopal episodes or known EKG abnormalities.

Physical examination was unremarkable except for obesity, a widely split second heart sound, a uterine size of three months' gestation, and 2 large ecchymoses of her left face. Her admission electrocardiogram showed striking left axis deviation and complete right bundle branch block and when repeated, showed variable second degree A-V block with conducted beats showing both left and right bundle branch block configuration (Fig. 1).

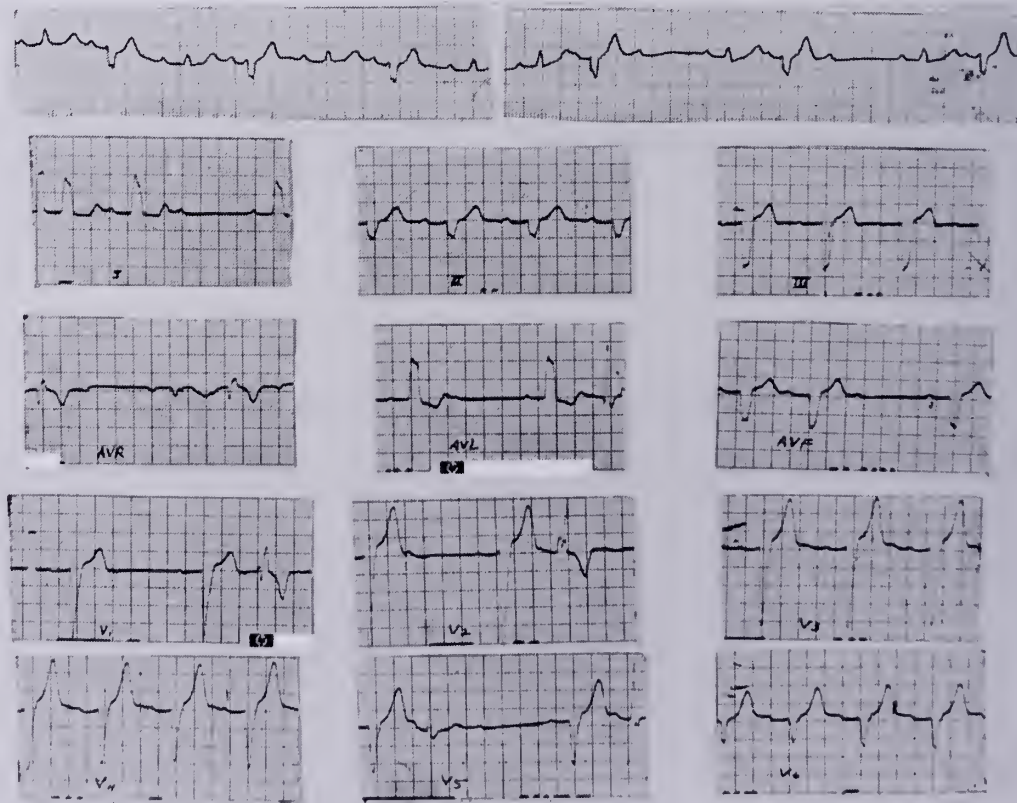


Fig. 1

*Fellow in Cardiology. Now at Los Alamos Medical Center, Los Alamos, New Mexico.

**Lovelace-Bataan Medical Center, Section of Cardiology, and University of New Mexico School of Medicine. Reprint requests should be addressed to Dr. Conrad, 263 State Street, Bangor, Maine.

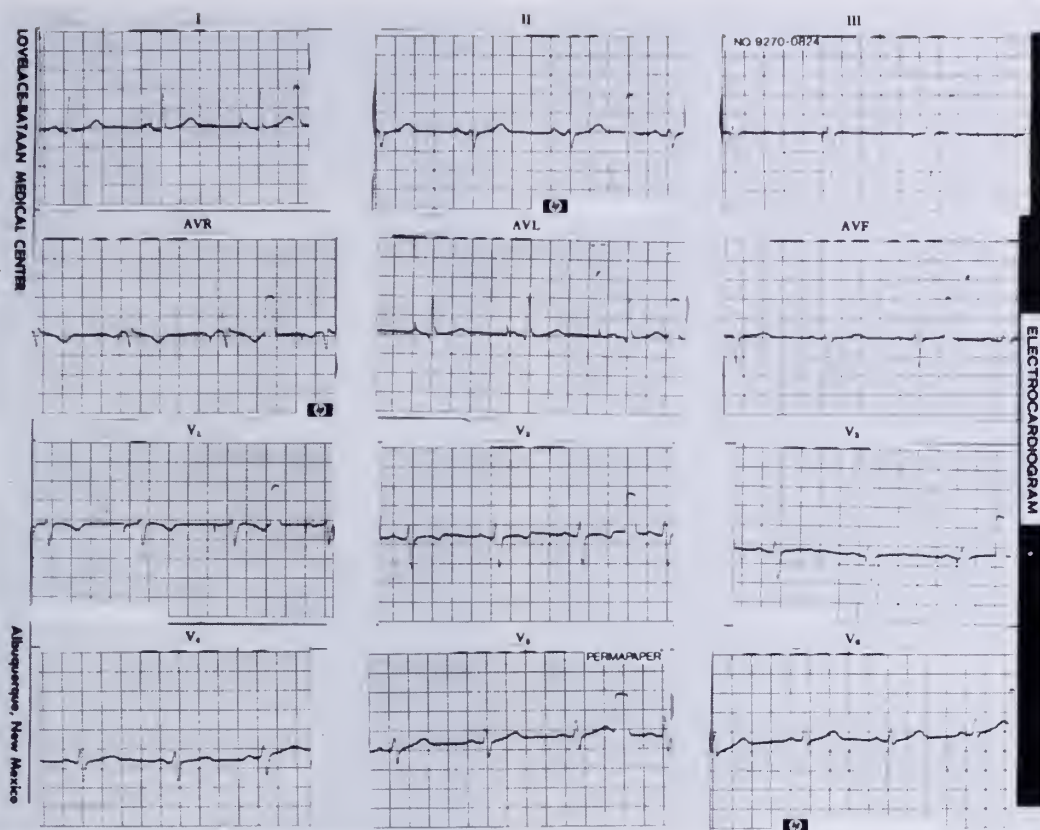


Fig. 2

Complete A-V block with syncope ensued while temporary electrical pacing was being instituted. HIS bundle studies were not carried out at this time. An extensive laboratory work-up revealed no important abnormalities and the etiology of her block remained uncertain.

After five days of temporary pacing, during which diagnostic studies were obtained, the patient underwent uneventful implantation of a demand impulse generator (Medtronic 5942), with epicardial leads (Medtronic 6914). At surgery the heart, pleural and pericardial surfaces were normal to gross inspection. In July 1972, her electrocardiogram had reverted to normal except for a frontal plane axis of -40 degrees, and remains unchanged (Fig. 2). In September 1972, pacemaker failure was discovered, and chest x-ray showed fracture of both spring electrodes near the myocardial surface; however, the patient, working full time as a school teacher, was totally asymptomatic and remains so to date. Out-patient monitoring (Avionics) has demonstrated no recurrence of either intraventricular or atrioventricular conduction defects.

HIS bundle electrograms in September 1972, prompted by the discovery of pacemaker failure, demonstrated A-H interval of 100 msec. and H-V interval of 50 msec. These intervals remained normal after 2 mg. of intravenous atropine which increased the rate to 110 beats per minute.

DISCUSSION

Histopathologic studies of patients with non-surgical trifascicular block have identified fibrosis of the His Purkinje system as a principle causal factor.^{2,3} The patients considered in such studies are

usually in an older age group or have obvious coronary artery disease. A less common cause, which Schaal has recently reported, is familial trifascicular disease.⁴ The relative youth of our patient, the temporary nature of her block and the lack of a positive family history would indicate that the underlying process was not one usually encountered, and would suggest a self limited, perhaps inflammatory process. Although initially the seriousness of her clinical picture demanded the use of permanent pacemaking, this was later abandoned when spontaneous improvement became apparent. A longer period of follow-up will add to our certainty regarding the probable temporary nature of her disease process.

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Villous Adenoma of the Colon With Severe Fluid and Electrolyte Depletion

Report of a Case

H. CLEMENT JURGELEIT, M.D.

Villous tumors of the large bowel frequently present with a mucus diarrhea. A long history of a profuse mucoid rectal discharge without impairment of general health is suggestive of this lesion. The syndrome of severe fluid and electrolyte depletion secondary to a villous adenoma is uncommon. Since its first description by McKittrick in 1954,⁷ there have been several series of collected case reports documenting this potentially lethal situation.^{1-3,8-11} The purpose of this report is to present an additional patient with this condition, somewhat complicated by underlying Addison's Disease.

REPORT OF A CASE

A 64-year-old woman presented in April 1975 with a ten-year history of watery mucoid diarrhea, five to eight movements per day. Following a syncopal episode in January 1975, she was noted to be pigmented and was given hydrocortisone with a tentative diagnosis of Addison's Disease. During this hospitalization, the BUN ranged from 70 to 90 mg%, the serum sodium 120 to 125 meq/l and the serum potassium 2.5 to 3.0 meq/l. Because of progressive weakness, she was referred to the Eastern Maine Medical Center in April 1975.

The physical examination on admission was essentially unremarkable except for the obvious skin pigmentation. Admission BUN was 40 mg%, sodium 131 meq/l, potassium 3.1 meq/l and chloride 83 meq/l. Subsequent endocrine work-up did indeed reveal mild hypoadrenalism.* Replacement glucocorticoid and mineralocorticoid therapy was instituted. The diarrhea, however, continued unabated with measured volumes 3000 to 5000 cc/24 hr. Despite periodic intravenous supplement, she became severely dehydrated and lethargic with marked electrolyte imbalance, and one week after admission the BUN was 192 mg%, the sodium 110 meq/l, potassium 2.8 meq/l, chloride 70 meq/l and total carbon dioxide 10 meq/l. This was promptly corrected by aggressive intravenous fluid and electrolyte replacement. Lower gastrointestinal work-up revealed a massive villous lesion in the rectosigmoid colon occupying the entire circumference of a dilated bowel, extending from ten to eighteen cm on proctosigmoidoscopic examination. Multiple biopsies were benign. The

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lesion on barium enema examination is shown in Figure 1. A low anterior sigmoid resection was performed on April 22, 1975. The gross pathology specimen showed a ten x eight cm giant villous adenoma (Figure 2A, and 2B) which, on microscopic examination of multiple sections, was benign.

The resection was curative; by the time of discharge she was having one to two soft, formed stools per day. She went home with normal blood chemistries on maintenance steroid medication for the Addison's Disease.

DISCUSSION

Mucus diarrhea and bleeding are the two major presenting symptoms of a villous adenoma.^{4,6} The former may be profuse, but rarely is it severe enough to produce the depletion syndrome of dehydration, hyponatremia, hypokalemia, hypochloremia, prerenal azotemia, metabolic acidosis, and circulatory collapse. In the series reported by Shnitka,¹¹ nine of eighteen patients presented in a moribund state and three died. Daily diarrheal volumes of 2000 to 5000 cc were recorded. Without a history of diarrhea, the frequent differential diagnosis includes diabetic coma and adrenal insufficiency. It is interesting that this case also had underlying Addison's Disease.

Patients with this syndrome can often keep up with their fluid and electrolyte losses for years by marked increases in oral replacement. Only when the diarrheal volumes exceed 1000 to 1500 cc/day does the patient seem to fall behind and become progressively depleted.

The normal rectal losses are 100 to 200 cc/day with sodium and potassium concentrations of 2 to 5 meq/l and 10 to 15 meq/l respectively. The rectal fluid in this villous tumor diarrheal state contains isotonic levels of sodium and chloride, and a ten to fortyfold increase in potassium concentration (15 to 80 meq/l). A secretion of potassium is hypothesized.^{2,4,11} As the lesions causing this syn-

*ACTH STIMULATION TEST

24 hr. Urine Collection	17-Ketosteroid (6-18 mg/24 hr, normal)	17-Hydroxycorticosteroid (1-10 mg/24 hrs, normal)
Day #1 (baseline)	6.1	2.5
Day #2 (baseline)	4.1	2.6
ACTH 40 u IV		
Day #3 (1 day post ACTH)	4.9	6.3
Day #4 (2 day post ACTH)	8.6	12.8



Fig. 1. Barium Enema examination showing the large extensive lesion in the rectosigmoid colon.

drome are all large with vast secreting surfaces, large volumes are produced; and as they are all in the rectum or rectosigmoid colon, there is little remaining bowel for reabsorption.

SUMMARY

A case report of severe fluid and electrolyte depletion from a massive villous adenoma of the rectosigmoid colon is presented. The syndrome is discussed, and the often insidious presentation and life-threatening aspects are emphasized.

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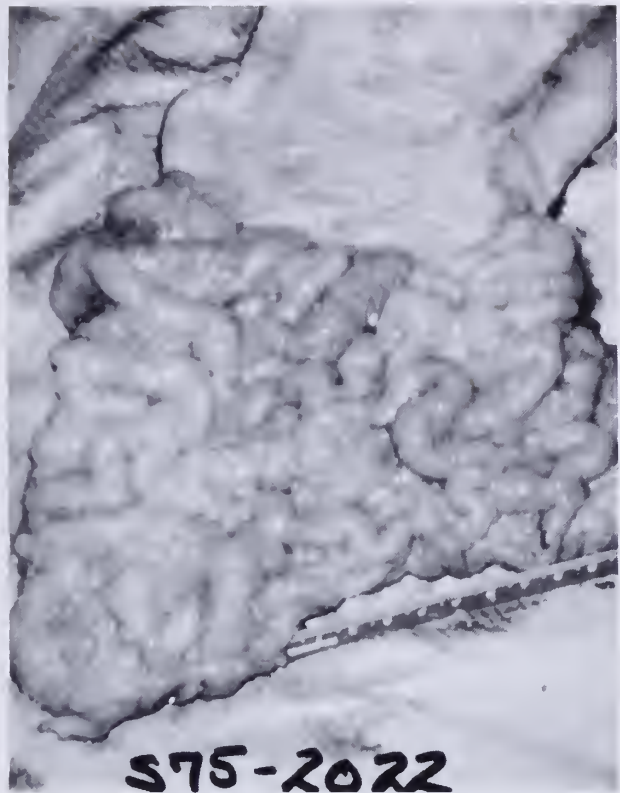


Fig. 2A. Massive Villous Adenoma of Rectosigmoid.



Fig. 2B. Close-up view of specimen in Figure 2A.

Treatment of Women Presenting With Incurable Breast Cancer

ALAN W. BOONE, M.D.*

Eleven women with advanced, essentially inoperable breast cancer at the time of diagnosis have been treated at the Eastern Maine Medical Center in the past three years. Almost all of these patients came to medical attention through symptoms related to a bulky breast tumor which either had become painful or which had ulcerated and bled. Five women had Manchester Stage III disease with advanced primary tumor, involvement of supraclavicular nodes, satellite skin nodules or fixation of tumor or nodes, and six had Stage IV disease with distant metastases. The patients were treated with a variety of palliative measures and most of them have done well. Although the number of patients is too few to be statistically convincing, our medical oncology group shares the belief that estrogen therapy, with or without chemotherapy, is preferable to surgery or radiotherapy as primary treatment in the elderly, postmenopausal patient who presents with Stage III or IV breast carcinoma.

If one defines a regression as six months of cessation of symptoms with objective decrease in disease and no appearance of new lesions, five of six such women so treated attained this happy result (see table). The one patient who did not experience regression (Case #10) suffered from progressive bony metastases and did not experience progression of the breast lesion. Our limited experience with radiotherapy alone or in combination with surgery as primary treatment (Cases 8 and 11) is not as encouraging.

Younger women presenting with advanced breast cancer were fewer in our group. Aggressive treatment including local irradiation or palliative breast surgery, and surgical ablation of ovarian and adrenal function may lead to excellent and sustained regression of disease (Cases 6 and 7).

Crile has recommended avoidance of palliative surgery in the patient presenting with Stage III or IV breast cancer, reserving conservative operations for selected cases.¹ Based on the experience of the Cleveland Clinic, he has advocated radiotherapy as the primary form of treatment in Stage III disease, reserving hormonal treatment and chemotherapy for relapsed Stage III and Stage IV cancer.

Common experience has led us to expect that ad-

ministration of estrogens to the postmenopausal patient with advanced breast cancer will yield a remission rate of 25 to 40%.^{2,3,4} It is perhaps not as widely appreciated that in patients in their late sixties and older, responses are more frequent and last longer.

One of the most gratifying advances in the treatment of breast malignancy in recent years has been the discovery that combinations of antineoplastic drugs are more effective than single agents used sequentially. Cooper was able to report 80% responses in sixty cases treated with a combination of fluorouracil, cyclophosphamide, methotrexate, vincristine and prednisone.⁵ Subsequent studies have reported lower response rates with the same or similar combinations, from 42 to 69%. Again it is noteworthy that older patients have responded better than younger, and those who responded to estrogens initially also had longer responses to combination chemotherapy than those who were estrogen-resistant.

The treatment of metastatic breast cancer has received much attention in the medical literature in recent years, but the treatment of a peculiar type of breast cancer, namely the elderly woman presenting with advanced primary neoplasm, has not received the attention it deserves. Crile's assertion that palliative resection of incurable breast cancer is rarely indicated is good advice. Our limited experience leads us to believe that medical treatment, i.e., estrogens and chemotherapy, may be preferable to radiotherapy in Stage III disease, and that radiotherapy to the breast in Stage IV disease is rarely needed.

In a review of five years' experience in treating breast cancer at the Lahey Clinic, Oberfield has stressed the desirability of a multidisciplinary approach.³ Nine of the eleven patients in this small series were presented in our weekly multidisciplinary oncology conference attended by medical oncologists, a surgeon, a radiotherapist and a pathologist. The other two were not and had Stage III disease treated primarily by palliative surgery or radiation. Treating the complex case of advanced breast cancer after such a conference may avoid the "blind men describing an elephant" situation where the patient receives a type of therapy determined, in large part, by the type of specialist she first sees.

Incurable breast cancer, especially in the elderly woman, does not necessarily mean that the patient

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**TREATMENT AND RESPONSE IN PATIENTS WITH INITIALLY-INCURABLE BREAST CANCER
EMMC 1972-1975**

Patient	Age at Diagnosis	Menstrual Status	Stage	Treatment	Regression & Duration (Mos.)	Survival to Date (Mos.)
1.	74	P	III	H+C	Yes, 37 & Continuing	39
2.	93	P	III	H	Yes, 25 & Continuing	26
3.	70	P	IV	H+C	Yes, 24 & Continuing	26
4.	77	P	III	H+C	Yes, 23 & Continuing	24
5.	77	P	IV	H+C	Yes, 18 - - - -	22†
6.	50	M	IV	S+A+C	Yes, 17 & Continuing	21
7.	37	M	IV	S+A+C	Yes, 15 & Continuing	17
8.	75	P	III	R	No	17
9.	73	P	IV	R+S+H+C	Yes, 6	11
10.	85	P	IV	H+C	No	11
11.	76	P	III	S+R	No	7

Abbreviations used in table are: P and M refer to more than five years postmenopausal and menstruating or at the menopause respectively; H refers to additive estrogen therapy; C to chemotherapy; S is breast surgery more extensive than biopsy; and A refers to ablative endocrine surgery; R refers to radiotherapy; † indicates the one patient who died before Sept. 1975. Notation: "& Continuing" refers to continuing regression as of this date.

is doomed to progressive suffering and a hasty demise. Ten of our eleven patients are alive seven to thirty-nine months following diagnosis, and many of them are asymptomatic. Simple medical treatment alone, or in conjunction with radiotherapy and surgery, may provide many months or even years of comfort.

ACKNOWLEDGEMENT

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Special Article

Perinatal Mortality Rate — Use as an Obstetric Indicator

PARKER F. HARRIS, M.D.*

INTRODUCTION

The now famous "Ten Goals in Ten Years" program of the American College of Obstetrics and Gynecology which was spelled out in 1973 by Keith Russell, M.D., FACOG, the 24th President of the ACOG in his inaugural address, has as a goal the reduction of the United States infant mortality rate to 10 per 1000 live births.¹ Infant mortality comprises neonatal (under 28 days) and post-neonatal (28 to 365 days) mortality and represents social as well as medical problems.² Currently, as is presented in the ACOG publication *Standards for Ob-Gyn Services* (1974), an indicator of Obstetric care as it relates to the infant mortality rate comes from the computation of the perinatal mortality rate.³ Determination of the perinatal mortality and efforts toward reduction of the rate support the goal of infant mortality rate improvement.

PERINATAL MORTALITY RATE

The perinatal mortality rate is the number of still-born infants and neonatal deaths per 1000 total births. Generally, included as stillborn infants in the United States are those weighing 500 grams or more and/or ones of a gestation of 20 weeks or more. Some institutions use 1000 grams or more. The neonatal period is broken into sub-groups I, II, or III for the first 24 hours, 24 hours to 7 days, and 7 to 28 days. The value is, also, often shown for neonates of different weight groupings, i.e., 500 to 999 grams, 1000 + grams, 1500 +, etc. The Basic formula is:

$$\frac{\text{Perinatal Deaths (neonatal plus stillborn)}}{\text{Liveborn Infants + Stillborn Infants}} \times 1000$$

The International definition includes stillborn infants of 28 completed gestational weeks and neonatal deaths from birth through 7 days. Comparison of perinatal mortality rates must be done with consideration of the variables mentioned.⁴

SUMMARY OF A HOSPITAL EXPERIENCE

The Wesson Women's Hospital in Springfield, Massachusetts has approximately 5000 Obstetrical

deliveries per year. Perinatal mortality is calculated there for stillborn infants of 1000 grams or more and includes neonatal deaths under 7 days. Perinatal mortality in 1970 was 23.4/1000, 18.6/1000 in 1971, 13.5/1000 in 1972 and 12.2/1000 in 1973. At the same time, neonatal mortality was 8.25/1000 in 1970, 7.33/1000 in 1971, 2.4/1000 in 1972, and 4.1/1000 in 1973. Marked improvement in the neonatal rate occurred during the year following the opening of a Special Care Nursery. The absolute values are of interest and give an idea of the levels that can be obtained. But, of relevance to this paper are the trends demonstrated by the perinatal mortality rates which can lead to fulfillment of the ACOG Goals.⁵

DISCUSSION

The perinatal mortality rates are used to gauge Obstetric care. Reduction of these rates is the concern of all Physicians caring for pregnant women. Recent concepts of care help focus attention on particular conditions relating to pregnancy which may be amenable to intervention and help to identify areas of Physician and Patient responsibility. The concept of "High Risk" pregnancy management⁶ and the practice of dating of the pregnancy in weeks of gestation from the first day of the last menstrual period instead of the less specific months of gestation have been particularly useful. Four areas were noted as needing special attention in the Massachusetts Medical Society Committee on Perinatal Welfare Study of 1971. These were postmaturity, fetal distress, Rh disease, and diabetes.⁷ Recommendations from the same study included the need for regionalization of facilities, "high risk" mother identification, development of transport systems, provision of consultation services, educational program development, and birth and death certificate matching. Also recommended and particularly applicable to this discussion, was that perinatal mortality rates adjusted for pertinent factors be tabulated for all maternity services and communicated to each other on a regular basis, and that all maternity services have a perinatal mortality committee which would form the basis for peer review.⁸

CONCLUSION

The ACOG "Goals" have been set and implemented.
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The Clinical Use of Digitalis Glycosides

DAVID H. HUFFMAN, M.D.

ABSTRACT

A significant number of patients who receive digitalis develop toxicity. Through an increased understanding of the clinical pharmacology of these drugs, a careful consideration of the clinical indications for using the digitalis glycosides, an increased effort to individualize therapy, and diligent monitoring of patients for clinical response and toxicity, it is hoped that the number of toxic events will be decreased.

The digitalis compounds are among the most frequently prescribed drugs. Since 10 to 20% of the patients receiving digitalis will develop signs or symptoms of digitalis toxicity, the digitalis compounds are among the most frequently encountered drugs in surveys of drug toxicity.^{1,2} Through an increased understanding of the clinical pharmacology of these drugs, it is hoped that the number of toxic events due to digitalis will be decreased. Part of this reduction will result from a more rational individualization of digitalis therapy. This individualization should include not only a choice of the proper dose of digoxin or digitoxin for the patient, but also a careful examination of the clinical indications for therapy with the cardiac glycosides.

Digitalis compounds are usually prescribed for two problems: (1) ventricular rate control in patients with atrial fibrillation or flutter, and (2) treatment of congestive heart failure. The use of digitalis to control ventricular response in the presence of supraventricular arrhythmias is well established. Therapy with digitalis in this condition is more precise than it is in the treatment of congestive heart failure since the ventricular rate is easily determined and can be used to individualize therapy. In contrast, treatment of congestive heart failure with digitalis, while

usually effective, is less precise and more controversial.³ After reviewing the clinical pharmacology of the digitalis compounds, the clinical use of the cardiac glycosides will be discussed with particular attention to the selection of patients for digitalis therapy and to a study of the usefulness of various methods to monitor digitalis therapy.

PHARMACOLOGICAL PROPERTIES

A detailed review of the basic pharmacological properties of the digitalis compounds is beyond the scope of this review and the reader is referred to recent reviews on this subject.⁴⁻⁶

The principal effect of digitalis is to increase the force of myocardial contraction. This inotropic effect makes digitalis useful in the treatment of congestive heart failure. In addition to the inotropic effect, digitalis has a number of electrophysiological effects on the heart, including alterations in automaticity, excitability, conduction velocity, and refractory period.

The decreased rate of impulse propagation through the atrioventricular (AV) node makes digitalis particularly useful in controlling ventricular rate in patients with atrial fibrillation. The electrophysiological effects of cardioglycosides are related to the inhibition by digitalis of the ($\text{Na}^+ - \text{K}^+$) activated ATPase system. This system is responsible for maintaining the normal electrolyte gradients across the cell membrane. The inotropic effect of digitalis appears more closely related to changes in the intracellular calcium flux. Digitalis increases the fraction of rapidly exchangeable calcium which is in turn related to myocardial contractility. It is possible that the inotropic effect of digitalis is more closely related to calcium homeostasis and that the cardio-toxicity is more closely related to the inhibition of the ($\text{Na}^+ - \text{K}^+$) ATPase system. These two effects, however, are related since the intracellular cation concentration, which is maintained by the ATPase system, is an important determinant of calcium flux.

Digitalis increases the automaticity of the cardiac cells by a reduction in the resting membrane potential through inhibition of the ATPase system. It is important to distinguish between excitability and automaticity since increased premature beats leading to ventricular tachycardia occur when there is a successive reduction in ventricular excitability.

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Increased automaticity and decreased conduction velocity in the presence of reduced excitability and the tendency for reentry phenomena are the events which initiate the ventricular fibrillation of digitalis intoxication.

An additional clinically important effect of digitalis is on myocardial oxygen consumption. The effect of digitalis on oxygen consumption depends upon the hemodynamic state of the patient. In a patient with congestive heart failure, digitalis increases both the force of the contraction and the rate of development of the contraction force. This is associated with a decrease in the left ventricular end-diastolic pressure and volume and a shift of the left ventricular function curve toward normal. In the patient with a dilated-failing heart, the increased cardiac output due to digitalis occurs without an increase in myocardial oxygen consumption, since the cardiac work required to produce a certain cardiac output is less with a small ventricle than in a dilated-failing chamber. In contrast, in patients without congestive heart failure, the myocardial oxygen consumption will be increased by digitalis. In this clinical setting, the patient receiving digitalis may experience exacerbation of angina pectoris if coronary insufficiency is present.

PHARMACOKINETICS

The clinical pharmacokinetics of the cardiac glycosides have been recently reviewed in detail.^{4,7,8} The principal differences between digoxin and digitoxin, the two most commonly used cardiac glycosides, are summarized in Table 1. A number of studies in the recent literature confirm the original observations by Smith, et al⁹ that a correlation exists between serum digitalis concentration and clinical digitalis intoxication. Since the serum concentration is correlated with clinical response, it is important to understand the factors which determine the serum digitalis concentration. Wagner and associates¹⁰ have determined the following relationship.

$$\text{"Steady State" Drug Concentration} = \frac{\text{Dose} \times \text{Fraction Absorbed} \times \text{Half-Life} \times 1.44}{\text{Apparent Distribution Volume} \times \text{Dosing Interval}}$$

This relationship is helpful in understanding the contribution of the various pharmacokinetic parameters to the steady state digitalis concentration. "Steady state" conditions are usually achieved after four to five half-lives have elapsed in the patient on maintenance therapy. Although a loading dose may be used to achieve this steady state concentration more rapidly, the steady state concentration is a function of the maintenance dose rather than the loading dose.

Digoxin, in contrast to digitoxin, is incompletely absorbed. Based on single dose studies, the elixir is

TABLE 1

PHARMACOKINETIC PARAMETERS		
	Digoxin	Digitoxin
Absorption	50-80%	90-100%
Average Half-Life	1.7 days	7 days
Renal Excretion	++++	+
Hepatic Metabolism	+	++++
Protein Binding	25-30%	86-94%
Therapeutic Level	0.9-2.2 ng/ml	12-28 ng/ml
Toxic Level	> 3 ng/ml	> 35 ng/ml

80 to 85% absorbed.¹¹ When digoxin tablets are administered, absorption is less than the elixir.^{11,12} The percent of digoxin absorbed from a digoxin tablet has been referred to as its bioavailability. Digoxin tablets made by different manufacturers have had widely varying bioavailability,¹³⁻¹⁵ which is related to the in vitro dissolution of the digoxin tablet.^{16,17} This indicates that the way the digoxin tablet is manufactured is an important determinant of how well the digoxin is absorbed from the tablet. Hopefully, variations in bioavailability will be reduced by the guidelines recently issued by the Food and Drug Administration.¹⁸ Malabsorption due to mucosal abnormalities,¹⁹ gastrointestinal irradiation,²⁰ alteration in gastrointestinal motility²¹ and neomycin,²² among others, have been shown to decrease the absorption of orally administered digoxin. The bioavailability of the digoxin preparation is an important determinant of some of these influences since improved bioavailability has been shown to eliminate the effects of irradiation²⁰ and gastrointestinal motility²³ on the oral absorption of digoxin.

The intramuscular administration of digoxin is associated with incomplete and erratic absorption.²⁴ Moreover, considerable pain as well as elevations in serum creatinine phosphokinase are associated with the intramuscular injection of digoxin. Hence, the intramuscular administration of digoxin is not recommended.

Due to differences in the rate of metabolism, protein binding, and renal excretion, the elimination half-lives of digoxin and digitoxin are considerably different. The half-life of digoxin in patients with normal renal function is 1.3 to 2.0 days. Digoxin is filtered at the glomerulus and not significantly reabsorbed by the renal tubule. As demonstrated in Figure 1, there is a substantial correlation between digoxin clearance and creatinine clearance. A similar relationship has been demonstrated between the renal clearance of urea and digoxin.²⁵ Since renal clearance is the major route of elimination of digoxin from the body, a progressive decrease in renal clearance of digoxin is correlated with a prolongation of the half-life of elimination. Thus, if renal function is impaired in patients on digoxin, the half-life will be increased and accordingly there will be

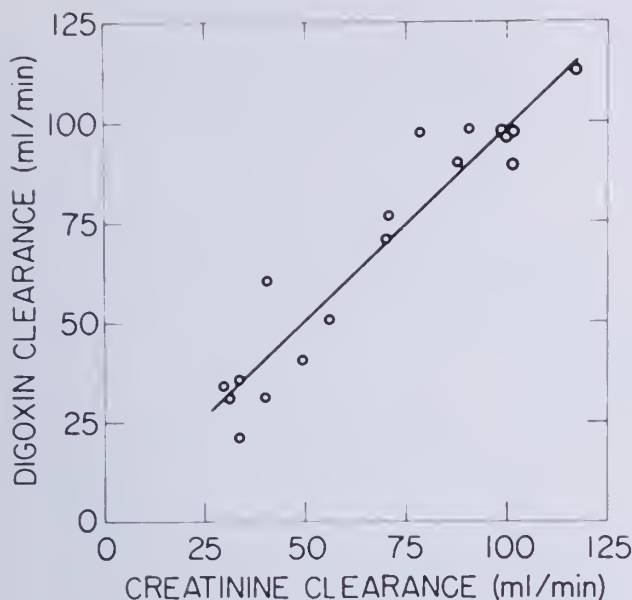


Fig. 1. The correlation between digoxin and creatinine clearance. The digoxin clearance was determined during the last four hours of the dosing interval in patients on maintenance digoxin therapy.

an increase in the steady state digoxin concentration if no alterations are made in the dose or dosing interval.

Due to a low renal clearance of digitoxin, alterations in renal function do not significantly affect the half-life of elimination of digitoxin. Digitoxin is less polar than digoxin and is bound to plasma proteins to a greater extent than digoxin. In addition, digitoxin is metabolized more than digoxin. A larger percentage of digitoxin, about 25 to 30%, undergoes an enterohepatic circulation. This recycling of digitoxin contributes to the longer terminal half-life of digitoxin. Interruption of this enterohepatic circulation by either biliary fistula or by administration of an anion exchange resin such as cholestyramine²⁶ will result in a decrease of the half-life of elimination for digitoxin. The latter has been employed to treat clinical digitoxin intoxication. Although the enterohepatic cycling of digoxin has been assumed to be small, approximately 8% of the dose,²⁷ recent studies by Caldwell, et al²⁸ indicate that the enterohepatic cycling of digoxin may be considerably greater than earlier estimates. If substantiated, the use of an anion exchange resin may also be useful in the treatment of digoxin intoxication.

The digitalis compounds are widely distributed in the body. The volume of distribution of digoxin is proportional to lean body mass, with muscular individuals having a larger distribution volume than obese individuals based on body weight. The apparent distribution volume of digoxin is quite large and probably represents an important source of variability in relating the digoxin dose to the steady

state blood level. Although the various factors which influence the distribution volume of digoxin are imperfectly understood, some information is available. In addition to lean body mass, thyroid²⁹ and renal function³⁰ are important determinants of the distribution volume of digoxin. In hypothyroidism, the apparent distribution volume is smaller than normal, resulting in a higher steady state concentration. In contrast, hyperthyroid patients have an increased volume of distribution. Despite these differences, the digoxin half-life of elimination was not affected by thyroid function.²⁹ Recently, we have demonstrated an increase in the biliary excretion of digoxin and its metabolites in hyperthyroid rats.³¹ This suggests that both the distribution volume changes and biliary excretion may be important determinants of the response to digoxin therapy in patients with altered thyroid function. In addition to the well known effect of renal insufficiency on the clearance of digoxin, it appears that renal failure may also decrease the apparent distribution volume of digoxin.³⁰ This change in distribution volume has been demonstrated by a decrease in the myocardial-serum ratio for digoxin in the presence of renal insufficiency.³² A substantial number of patients with renal insufficiency are hypothyroid.³³ This may explain, in part, the decreased distribution volume of digoxin in patients with renal insufficiency.

It is important to re-emphasize that the "digitalizing" or initial loading dose is not the ultimate determinant of the "steady state" concentration. This level, which is correlated with the clinical response, is achieved after chronic dosing for approximately five half-lives (about six to ten days for digoxin and 30 to 45 days for digitoxin) and will be determined by the maintenance dose, the dosing interval, the fraction of drug absorbed from the dosing form, the elimination half-life for the glycoside and the volume of distribution of the cardiac glycoside in that patient. This applies not only to the initial considerations, but also to subsequent monitoring of the individual patient. For example, if the patient's endogenous creatinine clearance decreases, there will be an associated prolongation in the digoxin half-life and an increase in the steady state digoxin level. This effect will not become completely manifest until four to five drug half-lives have elapsed following a significant change in the various parameters.

By understanding the various factors which determine the steady state digoxin concentration, it should be possible to more rationally individualize therapy with digitalis glycosides.

CLINICAL CONSIDERATIONS

Before using digitalis, it is important to consider the reasons for initiating therapy. If digitalis is used

to treat congestive heart failure, it is important to consider the differential diagnosis of congestive heart failure and, if possible, to define as clearly as possible why the patient is in congestive heart failure. Many forms of heart failure are poorly responsive to digitalis. These include high output failure, constrictive pericarditis and certain myocardiopathies. In an effort to treat CHF in these situations, the digitalis dose may be inappropriately increased and digitalis intoxication may occur. The second question is the choice of the cardiac glycosides. In recent years digoxin has been used with greater frequency than digitoxin. This is primarily because of its more rapid onset of action and shorter half-life as compared with digitoxin. There are many clinical circumstances, however, where digitoxin is a reasonable alternative to digoxin. Since digitoxin has a longer half-life, fluctuations in the serum digitoxin level will be less marked than they are with digoxin. Therefore, a missed dose will not result in a major change in the serum digitoxin level or in the clinical response. An additional advantage of digitoxin is its more consistent and complete absorption.

After choosing the glycoside, the clinician must determine how urgently the therapeutic effect is required. This depends in part upon the reasons for initiating therapy. The more rapidly a patient develops congestive heart failure, the more urgent is the need for digitalization. It is inappropriate to rapidly digitalize a patient who has insidiously developed congestive heart failure unless he presents with significant pulmonary edema. Prior to rapid digitalization, a physician should be certain about previous digitalis therapy. The radioimmunoassay can quickly answer this question if uncertainty exists. The dose response for digoxin occurs at low levels and as such there is no uniform digitalizing dose. The principal therapeutic objective in treating congestive heart failure is to administer the amount of digitalis which is required to achieve the desired inotropic effect. In general, 8 to 15 $\mu\text{g}/\text{kg}$, representing 0.5 to 1.25 milligrams orally over 12 to 15 hours, is adequate. This, however, may be too great a dose for the patient with renal failure or hypothyroidism since the distribution volume of digoxin is reduced in these patients. Since digoxin from tablet dosage form is incompletely absorbed, the digitalizing dose should be reduced by 25 to 40% if the drug is administered intravenously.

There are a number of factors which determine this maintenance dose. Many of these were outlined in the discussion under *Pharmacokinetics*. In Figure 2, the relationship between serum digoxin concentration and the dose of digoxin is given for patients after chronic oral dosing. This figure gives the regression lines correlating the maintenance

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IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or Narcan® (naloxone HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

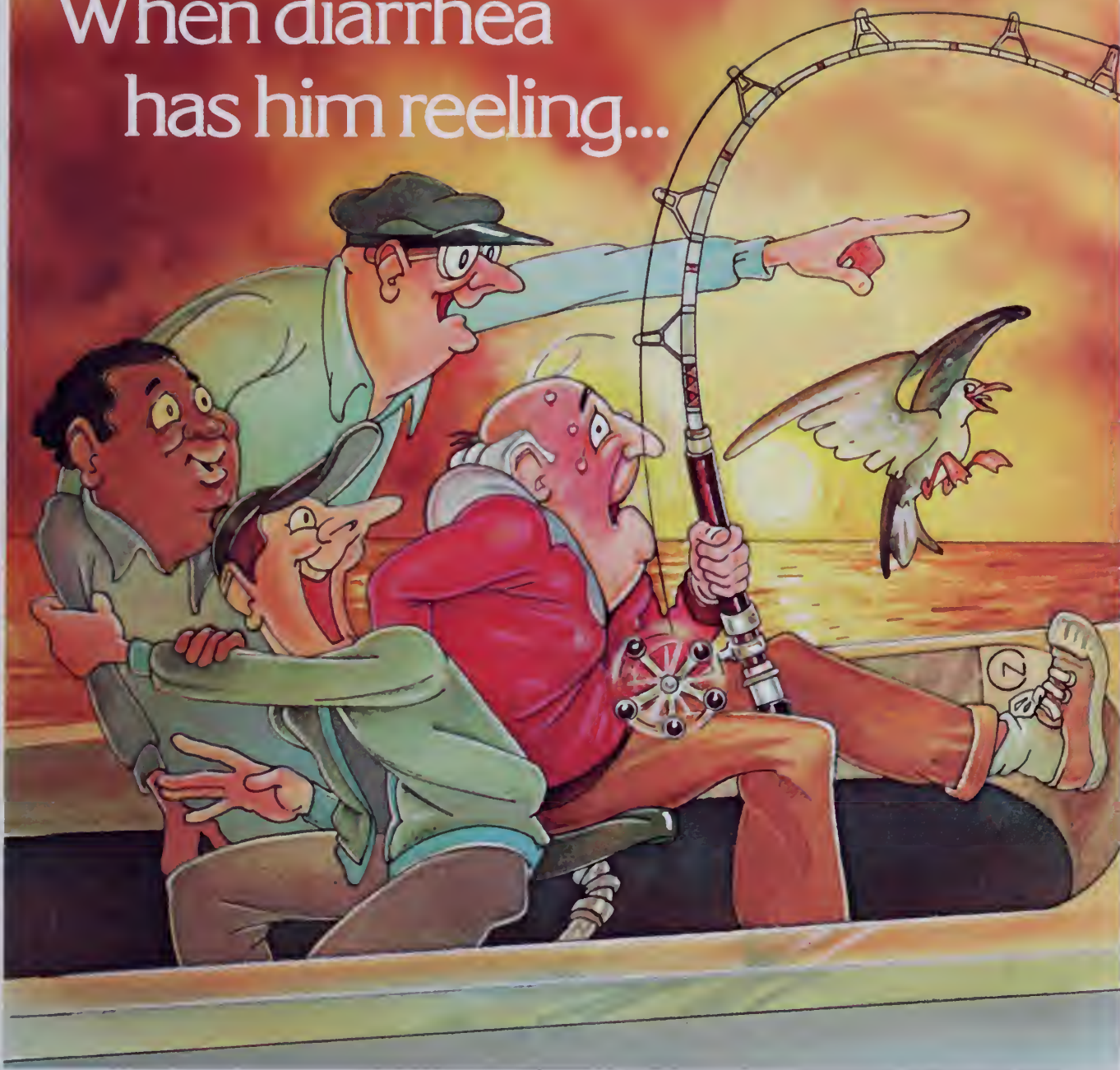
Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of 1/2 ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

SEARLE

Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Department, Box 5110,
Chicago, Illinois 60680

When diarrhea has him reeling...



Diarrhea can hook anyone. When it does, physicians and patients both want prompt control of diarrheal symptoms. Lomotil will usually control diarrhea promptly.

This rapid action can halt the emergency aspect of diarrhea and is comforting and reassuring to the patient. Electrolyte and

fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate specific therapy should be given along with Lomotil.

Lomotil is contraindicated in children less than 2 years old.

Lomotil[®]

TABLETS LIQUID

holds the line.

Each tablet and each 5 ml of liquid contain: diphenoxylate hydrochloride 2.5 mg (Warning: May be habit forming), atropine sulfate 0.025 mg

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration



Dr. James H. Sammons
Executive Vice President
of the American
Medical Association



The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

Opinion
&
Dialogue

main purpose of drug information for the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with this agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a long one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is

no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a pa-

tient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

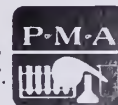
Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005





Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

- Found useful in the management of vertigo* associated with diseases affecting the vestibular system.
- Can relieve nausea and vomiting often associated with vertigo.*
- Usual adult dosage for Antivert/25 for vertigo:* one tablet t.i.d.
- Also available as Antivert (meclizine HCl) 12.5 mg. scored tablets, for dosage convenience and flexibility.
- Antivert/25 (meclizine HCl) 25 mg. Chewable Tablets for nausea, vomiting and dizziness associated with motion sickness.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

Effective: Management of nausea and vomiting and dizziness associated with motion sickness.

Possibly Effective: Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

CONTRAINDICATIONS. Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

WARNINGS. Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Usage in Children: Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

Usage in Pregnancy: See "Contraindications."

ADVERSE REACTIONS. Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

ROERIG 
A division of Pfizer Pharmaceuticals
New York, New York 10017

Antivert[®]/25
(meclizine HCl) 25 mg. Tablets
for vertigo*

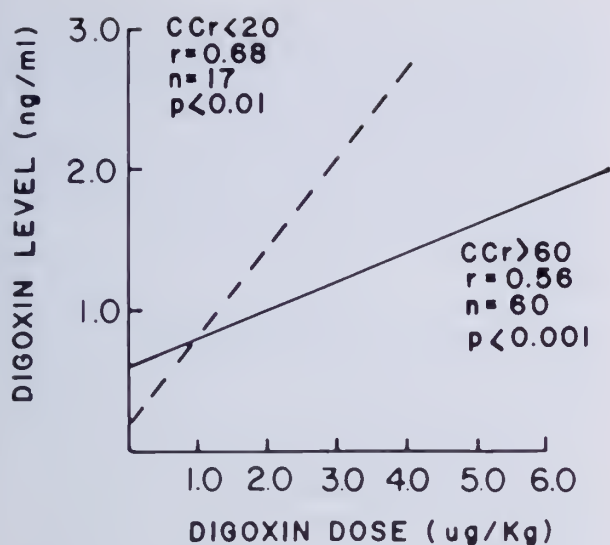


Fig. 2. The correlation between digoxin dose and serum digoxin level: Effect of renal function. The regression lines were determined for patients with normal renal function (—) and for patients with renal failures (---). The serum digoxin concentrations were measured 6-8 hours following the last digoxin dose in patients who were on maintenance digoxin therapy for at least one week. Abbreviations: CCr = creatinine clearance; r = the correlation coefficient for the regression line; n = the number of patients; and p = the level of significance.

digoxin dose with the digoxin level for patients with normal renal function and for patients with renal failure. There are two important differences in the dose response curves. First, the regression line is shifted to the left by poor renal function. If 1.4 ng per milliliter is the desired therapeutic level, the maintenance digoxin dose is 4 μ g/kg or 0.25 mg for a 63 kg individual. In contrast, to achieve the same digoxin level in a patient with renal failure, the dose is 2 μ g/kg or 0.125 milligrams. A second consideration is the slopes of the regression lines. Increasing the digoxin dose results in a greater increase in the serum digoxin concentration in the patient with renal failure than in the patient with normal renal function. This is probably related to the decreased apparent distribution volume for patients with renal insufficiency and may further help to explain why patients with renal insufficiency are more prone to develop digoxin toxicity.

A narrow margin exists between the therapeutic and toxic serum digoxin concentration.^{9,34,35} These original observations have been substantiated by several subsequent studies and indicate that a useful method for monitoring clinical response to digoxin is to measure the serum digoxin concentration. The serum for the digoxin concentration should be obtained six to eight hours after the last dose. In addition to demonstrating that there was a significant difference between therapeutic and toxic digoxin concentrations, we have recently evaluated patients who were not toxic but who were in congestive

heart failure in an effort to define a sub-therapeutic group. These patients had lower mean serum digoxin concentration than patients who had a therapeutic response.³⁶ Thus, the digoxin concentration is helpful in determining if a therapeutic effect can be anticipated. The therapeutic range for digoxin was 1.0 to 2.2 ng/ml at six to eight hours following a dose and is consistent with other reported ranges.³⁷

Because of the high incidence of digoxin toxicity, a number of methods have been devised to assist the physician in treatment of the patient. These include nomograms³⁸ as well as computer programs.

There has been recent enthusiasm for the use of computer-assisted programs to advise physicians on digoxin dosage regimens.³⁹ These programs use pharmacokinetic information and have been shown to decrease the incidence of toxicity.⁴⁰ However, recent studies⁴¹ indicate that initial enthusiasm for these programs must be modified. The use of computer programs which accept input subsequent to the original estimation may be more valuable.⁴² Although these programs and the nomograms are useful in initiating therapy, it is important to individualize therapy. It appears that the least expensive, and most reliable way to evaluate digoxin therapy is to determine the serum digoxin concentration. Evidence has been reported^{43,44} that the availability of the serum digoxin concentration is associated with a 50% reduction of clinical digoxin intoxication.

The serum digoxin concentration should not be determined routinely in every patient who receives digoxin. However, digoxin levels are useful in a number of situations. The clinician will find the serum digoxin level useful in deciding: (1) if the patient is taking the glycoside regularly, (2) if bio-availability problems exist with the dosage form, and (3) if an arrhythmia is due to the glycoside or intrinsic heart disease. Serum levels are also useful (1) in a patient for whom an adequate history cannot be obtained, (2) when the physician wishes to know whether or not the patient is receiving digoxin or digitoxin, and (3) to determine whether the patient can be given more than the maintenance dose he is receiving at the time the level was obtained. It is important wherever possible to determine the presence of other factors such as age, thyroid status, acidosis, hypokalemia, hypoxemia, hypomagnesemia, hypercalcemia, etc. All of these factors are important determinates of the response to digoxin in the individual patient, and they may alter the expected clinical response based on the serum digoxin concentration. Thus, clinical judgment remains an essential factor in determining appropriate therapy with digoxin.

A controversy exists regarding the use of digitalis in acute myocardial infarction. Animal experiments

indicate that digitalis is more likely to be associated with serious arrhythmias in acute myocardial infarction, and digitalis may extend the infarct size. Clinical studies, however, support the judicious use of digitalis in acute myocardial infarction if the clinical indications for its use are present (supraventricular tachyarrhythmias, or congestive heart failure).⁴⁵ The use of digitalis in cardiogenic shock is unresolved. Although there are no strict dosing guidelines, it is suggested that one-half the dose of digoxin be administered. This clinical situation is an example where monitoring the serum digoxin concentration would be useful in individualizing therapy.

DIGITALIS TOXICITY AND ITS TREATMENT

In a recent prospective study of the 15% of patients taking digitalis on admission to a large hospital, 23% were found to have definite digitalis toxicity by serial electrocardiogram.³⁴ The importance of this problem is emphasized by a higher mortality rate in the patients with digitalis intoxication. The clinician must be constantly aware of the possibility of digitalis toxicity and obtain appropriate laboratory tests to substantiate the diagnosis. The most useful addition to the laboratory tests available for this purpose has been the digitalis radioimmunoassay which uses a specific antibody to the glycoside.⁴⁵ The accuracy and specificity of digoxin antibody are very important.^{46,47} The clinician must be aware of some technical problems, since they may affect the accuracy of the serum digoxin concentration measurement. These include quenching of the radioactive material by hemolyzed blood, the presence of hyperbilirubinemia, radioactivity in the patient's serum due to a diagnostic test, the interference by other drugs, such as spironolactone,^{4,49} with the binding of digoxin to the antibody, and the serum protein concentration.⁵⁰ The effect of these factors depends on the type of assay employed.

Criteria for clinical digitalis toxicity vary. Electrocardiographic changes are the most important toxic manifestations since they are associated with increased morbidity and mortality. Gastrointestinal and visual symptoms have been associated with digitalis toxicity. With the exception of anorexia, however, their correlation with the plasma digitalis concentration is poor.⁹ Since nausea and vomiting are caused by digitalis,⁵¹ the lack of correlation is most likely related to the association of these symptoms with cardiac failure, associated illnesses and other drugs.

The most frequently encountered arrhythmias include premature ventricular beats, usually bidirectional or coupled as bigeminy and trigeminy, atrial tachycardia with block, ventricular tachycardia or fibrillation and AV block [1st degree or

TABLE 2

FREQUENCY OF ARRHYTHMIAS IN DIGITALIS INTOXICATION

1. Ventricular Premature Beats — 33%
2. Ventricular Tachycardia — 8%
3. Non-paroxysmal AV Junctional Tachycardia — 17%
4. AV Junctional Escape Rhythms — 12%
5. Atrial Tachycardia with Block — 10%
6. Second and Third Degree AV Block 18%
7. SA Block with Sinus Arrest — 2%

TABLE 3

AN APPROACH TO THE PATIENT WITH SUSPECTED DIGITALIS INTOXICATION

1. Pre-disposing factors:
 - a. Is the dose too large?
 - b. Is the clearance of the drug reduced?
 - c. Are there factors which increase myocardial susceptibility to digitalis?
2. Are there extracardiac symptoms?
 - a. Anorexia,
 - b. Nausea or vomiting,
 - c. Visceral changes.
3. What is the cardiac arrhythmia?
4. What is the serum digitalis concentration?
5. Does the arrhythmia change when digitalis is withheld?

Mobitz Type I (Wenckebach phenomenon)]. In the presence of atrial fibrillation, additional clues to the possibility of digitalis toxicity include bradycardia, the presence of AV escape beats, AV junctional rhythm or the presence of a Type I exit block. Almost any arrhythmia can be caused by digitalis; accordingly, in a complicated clinical setting, it is often difficult to determine whether the arrhythmia is due to digitalis or not. The frequency of various arrhythmias encountered in digitalis toxicity is shown in Table 2. It is important, whenever possible, to document what happens to the arrhythmia when digitalis is discontinued. Disappearance of the arrhythmia after discontinuation of digitalis is important evidence that digitalis was the cause of the arrhythmia. There may be a period between the return of the serum digitalis concentration to therapeutic levels and the disappearance of the arrhythmia.

Acute digitalis poisoning may produce hyperkalemia resulting from the inhibition of the (Na^+ - K^+) activated ATPase system. The hyperkalemia is associated with a poor prognosis.⁵² This clinical setting is complicated since profound hyperkalemia can cause complete heart block and cardiac standstill. Thus, lowering the serum K^+ by such measures as glucose and insulin, and sodium polystyrene sulfonate (Kayexalate®) may be tried. However, care should be exercised to avoid hypokalemia and potentiation of digitalis toxicity. A temporary demand pacemaker is recommended in this clinical setting.

Early recognition of digitalis intoxication is essential to successful treatment. Treatment of the

digitalis arrhythmia is dependent upon the type of arrhythmia and the clinical setting in which it occurs (see Table 3). It is important, therefore, to individualize treatment with the various antiarrhythmic drugs. Often, careful electrocardiographic monitoring following discontinuation of digitalis is all that is required. In general, the conduction abnormalities are less life-threatening than those of increased automaticity since it often leads to ventricular fibrillation. The use of direct current shock to convert arrhythmia secondary to digitalis should not be used unless ventricular tachycardia or fibrillation exists. In particular, direct current shock to convert atrial fibrillation in a patient with digitalis intoxication is contraindicated. The risk of countershock is decreased when lower energy levels are used.⁵³

Phenytoin (diphenylhydantoin) and lidocaine are the agents of choice for the treatment of premature ventricular contractions and ventricular tachycardia.⁴ Phenytoin (DPH) can convert atrial tachycardia with blocked sinus rhythm and improve AV conduction. Although paroxysmal AV junction tachycardia may be abolished, it is usually more resistant to the effects of DPH. If the DPH is given intravenously, no more than 100 mg should be given every five to ten minutes with ECG monitoring until a satisfactory effect is obtained, or 1,000 milligrams is administered. Intravenous therapy is necessary since the half-life of DPH is approximately 24 hours and by simply giving 300 mg/day, four to five days would elapse before a therapeutic DPH concentration of 10 to 20 µg/ml was achieved.

Other forms of therapy for digitalis intoxication include potassium replacement, propranolol, quinidine and procainamide. These drugs are all less desirable since they decrease conduction and may potentiate the AV block produced by digitalis. New developments include the use of cholestyramine, colestipol and activated charcoal to interrupt the enterohepatic circulation of digitoxin. Digoxin may also undergo an enterohepatic circulation which is more extensive than was previously thought. Thus, the anion exchange resins, particularly colestipol, may be useful in the treatment of digoxin intoxication. Potassium canrenonate is currently an experimental approach for the treatment of digoxin intoxication. An additional experimental approach to the treatment of digitalis intoxication is its reversal by glycoside specific antibodies.⁵⁴ The use of Fab fragments, which have lower immunogenicity and a more rapid clearance than IgG molecule may one day be added to the methods for treatment of digitalis toxicity.⁴

CONCLUSION

The digitalis glycosides remain the most useful and reliable drugs for producing long-term increase of myocardial contractility, and they have a de-

served place in the treatment of congestive heart failure. In view of the high frequency of toxicity, however, it is important to consider the possibility that they may have been overused, particularly in the treatment of patients with symptoms suggestive of congestive heart failure, but in whom the reasons for congestive heart failure are poorly defined. Recent increases in our knowledge of heart failure indicate that a number of factors are important in producing this altered state of physiology. Among these factors are abnormalities in pre-load and after-load, which must be considered along with the abnormalities in contractility in deciding the therapeutic approach to the patient with congestive heart failure. It is hoped that through a better understanding of the mechanisms involved in altered myocardial contractility that a more rational basis can be chosen to individualize the need for the digitalis glycosides in the management of heart failure. The classical concept that heart failure is always an indication for digitalis therapy probably needs revision.³ It is also hoped that through understanding the clinical and basic pharmacology of the digitalis compounds that the clinical use of these drugs will become more rational and that, coincident with this increased rational use, there will be a reduction in the incidence of toxic events.

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PERINATAL MORTALITY RATE — USE AS AN OBSTETRIC INDICATOR

Continued from Page 346

mentation is in progress. Perinatal mortality rates are used to gauge Obstetric care. A hospital's experience is summarized. And, recommendations applicable to all Obstetric services have been presented.

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A Report of the International Symposium on pH and Blood Gases

WILLIAM H. AUSTIN, M.D.

On July 7th and 8th of this year, the National Bureau of Standards in Washington, D.C., sponsored a symposium in order to initiate a mechanism to handle the problems arising from the increasingly important fields of pH and Blood Gas Measurement.

Although it has been half a century since Van Slyke and Henderson described the physiologic relationships and mechanisms involved in acid-base balance, there still remain many uncertainties as to which indices are best measured, what parameters should be derived from the measured data and how to calculate them, and frankly, how these data should be interpreted by the clinician. It therefore is the goal of the American Association of Clinical Chemists, the National Committee for Laboratory Standards, and other interested researchers and clinicians to standardize the parameters in this field, so there may be a universal discourse and understanding of the many problems inherent in it. The conflict of ideas that still exists is serious, not only for the pedagogical need for uniformity and nomenclature, but also for the more pragmatic reason that as highly-sophisticated pH/blood gas analyzers are developed, the derived parameters upon which the clinician will base a large part of his diagnosis will be critically dependent upon the assumptions and "standard" values used in the calculations. Even as automated clinical acid-base analyzers are being developed, the unanswered significance of certain derived parameters and the need for standardization are problems that still remain.

At the request of these many interested parties, the United States Department of Commerce, through the National Bureau of Standards, took the initiative to sponsor a conference, in order to provide a forum for the resolution of the many and varied differences that exist, and to help establish acceptable, world-wide standards.

As an initial step, a panel of experts on pH and blood gases was assembled to deal with some urgent problems, and to establish a means for the formation of a group for continual study and recommendations in this area. Under the direction of Dr. Richard A. Durst, an intense conference was devised with participants from many countries, representatives from scientific societies, and scientists from three major instrument-manufacturing companies. This working panel of twenty-three members dealt with the following topics:

1. Acid-Base status
 - a. Definition of quantities and concepts
 - b. Recommendations of nomenclature, physiological terminology and symbols
 - c. Establishment of reference values
 - d. Evaluation of nomograms and algorithms
 - e. Establishment of methods for blood sampling, handling, and storage.

The balance of the session was concerned with:

2. Instruments, Methodologies and Standards
 - a. Instrument specifications
 - b. Quality control and standards
 - c. Development of reference methods

This was followed by open discussion which touched on the areas described. The transactions of this symposium are being published, and will serve as a working document for a Permanent Committee on pH and Blood Gas Measurement. Although there was no attempt made to completely resolve even the primary differences, progress was made by focusing on this subject at an international level.

For the clinician this means that there is some attempt being made to put this subject on a functional level, not only to help in the understanding of problems, but also with the communication of these problems on a common ground. For the researcher and basic scientist, it means the development of a uniform language, so that the exchange of ideas will not be hampered by a scientific language barrier.

As a participant, representing the United States, it was easy to see that the task was an enormous one. There is a strong European move to convert to the International System (S.I.)* of measurement, which would spill over into the medical field. This problem came on top of the already existing discrepancies in clinical and laboratory nomenclature and the physiological concepts which these encompass. The Bureau of Standards agreed to initiate work on the development of reference materials as a first step in the process of clarifying the many differences which are present.

It is the purpose of this report to assure the clinician who has to deal with these aspects of medicine more and more, that concerted efforts are being

*S.I. (Système Internationale): a relatively unfamiliar concept in the U.S., where such parameters as PCO_2 in mmHg would be spoken of as pKa (Pascal Units, i.e. $-7.5 \text{ mm} = 1 \text{ pKa}$.)

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A Burn Care Program For Maine

A Report to the Members of the Maine Medical Association

RICHARD C. BRITTON, M.D.*

With its 33,215 square miles and 993,000 people distributed in relatively few areas of density and coastal islands, Maine has serious problems with the transportation, definitive care, and rehabilitation of its seriously burned citizens. While the physical and emotional suffering of 400 hospitalized burn victims in Maine annually cannot be measured, the estimated cost to the Maine community exceeds \$500,000 in welfare support, aid to dependent children, workmen's compensation, loss of earned income, and loss of valuable manpower.

In 1972, a group of concerned individuals requested the Comprehensive Health Planning Agency in Augusta to determine the magnitude of the problem in the State. A Burn Study Group was appointed and a survey of the 50 acute care hospitals in Maine carried out in 1973. A report of these efforts was published in 1974.¹ The major findings and recommendations were as follows:

1. There are an average of 400 hospitalized burn victims in Maine each year with hospital length of stay ranging from less than one week to six months.
2. One hundred of these are seriously burned, require months or years of hospitalization and rehabilitation, and are usually referred to the two largest hospitals in the State.
3. Two-thirds of the seriously burned are adults for whom there is no center for burn care in the Northeast.
4. An average of ten badly burned children are referred from Maine each year to the Shriners Burns Institute in Boston. After superb burn center care, they are returned to Maine where deficiencies in special schooling and physical therapy exist.
5. There is no central coordination of existing resources for physical and vocational rehabilitation of the most frequently burned citizen, the male adult sustaining non-industrial burns.
6. No single Maine hospital has the capacity or resources to accept all major burn victims.
7. The volume of patients, initial and sustaining costs, and other considerations oppose the creation of a separate burn center for Maine.
8. The quality of acute burn care in Maine ranges from excellent to poor but the potential for a

uniformly high level of care is very real through a coordinated State-wide program.

9. It is recommended that the needs of Maine for improved burn victim care would be met best by a program of multiple strategically placed burn units, care provider training, central communication, and coordination of existing rehabilitation resources.

To carry out these recommendations, an Advisory Burn Committee was formed and sponsored by the Maine Medical Association. It includes wide representation by members of the Association, the Maine Hospital Association, the Maine Osteopathic Association, the Maine State Nurses Association, the Maine Industrial Nurses Association, the Maine State Federation of Firefighters, Maine Blue Cross and Blue Shield, the Union Mutual Insurance Company, the Liberty Mutual Insurance Company, the Maine Chapter of the Trauma Society, the Bureau of Health & Welfare, the Bureau of Labor & Industry, and the Comprehensive Health Planning Agency.

During the past two years, this committee has developed the following basic program:

1. The appointment of voluntary physician *Burn Officers* in each of the 50 acute care hospitals; their knowledge of acute burn management would be updated by periodic seminars conducted within the State and they, in turn, would instruct their own community medical and emergency room staffs.
2. The creation of four *burn units* to be located according to regional burn incidence, geographical position, population density, and local hospital interest. Tentatively designated are the Gould Memorial Hospital in Presque Isle (1 bed), the Central Maine General Hospital in Lewiston (3 beds), the Eastern Maine Medical Center in Bangor (4 beds), and the Maine Medical Center in Portland (4 beds). Each burn unit would have a *Director* administratively responsible for the development of a burn care protocol and the training of nurses and technicians.
3. The creation of a *central communications office* to provide assistance with daily burn census and patient referral, coordinate medical consultation, the recording of burn statistics, the planning of educational seminars, the coordination of physical and vocational reha-

*Secretary, Advisory Burn Committee of the Maine Medical Association. Address: 22 Bramhall Street, Portland, Maine 04102.

bilitation services, and cooperation with other agencies in public education in burn tion.

In late 1974, the Advisory Committee endorsed joint application with Emergency Medical Services for federal support of the program. However, cut-backs in this type of support eliminated burn care support and left a reduced amount of support for improvement of EMS services in mid-State. In early 1975, the interest of the Maine State Federation of Firefighters in helping with fund raising plans sparked renewed efforts culminating in a plan for major fund raising in 1976. This organization of 7,500 members represents the majority of active firemen in Maine of whom over 80% are volunteers. The Advisory Committee, after consultation with Dr. Hanley, is in the process of establishing an accountable tax-exempt vehicle for fund raising from public, State, and federal sources to be called the *Pine Tree Foundation for Burn Treatment*. The target of \$500,000 would be used to create the four properly equipped burn units, establish the central communication office, provide support for nurses and technicians sent to burn centers for special training, and to pay the costs of continuing education of all burn care personnel.

Hospitals approached in regard to participation in the program have been understandably reluctant to undertake new programs without guaranteed funding or to dedicate beds exclusively for burn care. It will be the responsibility of the Foundation to provide financial support for the costs of renovation and basic equipment, assistance with the costs of special training of personnel, and costs of continuing education. Costs of operating the central communication office, ideally located in one of the burn unit hospitals, would also be the responsibility of the Foundation. Clearly, burn unit beds must be

for multi-purpose use since variable burn patient census would otherwise make dedicated beds economically not feasible.

Physicians approached in regard to participation as burn officers have expressed concern that they would inevitably become responsible for the care of all burn patients admitted to their hospitals. While this could occur since the majority are surgeons who presently care for burn admissions, their primary function as burn officers would be educational at the local level. In addition, the assistance of trained burn technicians with time-consuming dressings and debridement will significantly reduce the surgeon's load, especially in hospitals without surgical house officers.

With the burn program fully under way, expected benefits for Maine include standardization of burn victim acute resuscitation and stabilization, a uniform high level of intermediate care of the majority of burn victims within the State, reduced length of stay through appropriate burn care protocols, and improved rehabilitation through coordination and expansion of existing services. Potential additional benefits resulting from cooperative efforts of the Advisory Committee, the Foundation, and Maine Master Plan for Fire Prevention, Control, and Administration would include more effective codes relating to flammable clothing for children and home fire extinguishers, more effective public education in firefighters. The success of the program, already endorsed by the Maine Medical Association in concept, hinges on continued support by the Association as sponsor and the membership as participants.

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A REPORT OF THE INTERNATIONAL SYMPOSIUM ON pH AND BLOOD GASES

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made to put the subject in proper perspective for better access in the treatment of his patient. This, after all, is what it's all about. It was clear to all of us that we were not dealing with "lab values," but with a kind of separate science (like electrocardiography, for example), where there is specialized help, better availability, and a usable, down-to-earth way of coping with pH and blood gas information. I do not mean to say that we have all the answers at our fingertips, but we do have concrete ways in mind to accomplish our goals. This first step will hopefully provide an initiative we have

long needed. I personally hope that soon we will not have to, with a straight face, tell our colleagues of such incomprehensible concepts such as "negative base excess" and the like.

The first fruits of our efforts, though very imperfect, will appear in book form and in journals this fall and winter. We ask your indulgence for a while, as with time things will take shape. With this also comes the pledge for our best efforts for you, and, foremost, the patient.

111 Westcott Rd., South Portland, Maine 04106

New Law Affects Every Physician

Sec. 1. 32 MRSA § 2806 is enacted to read.

§ 2806. Prescribing and dispensing of drugs.

Every written prescription issued by a physician, osteopath or dentist in this State shall contain in the lower right-hand corner of such prescription form a box at least ½ inch by ½ inch.

The following words shall appear to the left of this box: "Any drug which is the generic or chemical equivalent of the drug specified above in this prescription may be dispensed provided that the drug dispensed is listed in the current edition of either the National Formulary or the United States Pharmacopoeia and provided that no check mark (✓) has been handwritten in the box in the right-hand lower corner."

Any pharmacist receiving a prescription in which no check mark (✓) is found in the box provided is authorized to substitute a generic or chemically equivalent drug for the drug specified on the prescription, provided that the substituted drug is listed in the current edition of either the National Formulary or the United States Pharmacopoeia and that the price of the substituted drug does not exceed the price of the drug specified by the prescribing physician, osteopath or dentist.

Any pharmacist who substitutes a generic or chemically equivalent drug under the provisions of this section shall inform the person to whom the drug is dispensed of the substitution. Whenever any substitution is made under the provisions of this section, the pharmacist shall cause the name of the drug manufacturer or distributor to appear on the container label of the drug dispensed.

This section shall not apply to prescriptions ordered by physicians or osteopaths for patients in hospitals when such prescriptions are filled by a hospital pharmacy.

Sec. 2. Effective date. The effective date of this Act shall be January 1, 1976.

SAMPLE

SAMPLE

SAMPLE

PHYSICIAN'S NAME

B.N.D.D. #

CITY _____ STATE _____

FOR _____ DATE _____

ADDRESS _____

R

Any drug which is the generic or chemical equivalent of the drug specified above in this prescription may be dispensed provided that the drug dispensed is listed in the current edition of either the N.F. or the U.S.P. and provided that no check mark (✓) has been handwritten in the box in the right-hand lower corner.



_____ M.D.

Maybe the patient's self-diagnosis is right. He could have hay fever. But that bright red nasal mucosa, along with the thick discharge and excoriation around the nares, strongly suggests that the main problem is a cold. Hay fever or another form of allergic rhinitis may or may not be an underlying factor.

If a complete history and examination rule out allergic rhinitis, the long-term outlook will be a lot more favorable than his own "diagnosis" would have indicated.

But right now, whether he's got allergic rhinitis or a cold, he's suffering from the same irritat-

ing symptoms of drip, congestion and stuffiness. Try DIMETAPP EXTENTABS®. They're formulated to relieve these symptoms without much chance of causing drowsiness or overstimulation. Your patients will appreciate the 24-hour relief they can get from just one tablet every 12 hours.

Cold or



Allergy?

Whether it's a cold or an allergy, Dimetapp Extentabs® relieve stuffiness, drip and congestion.*

*

INDICATIONS

Based on a review of this drug by the National Academy of Sciences, National Research Council, and/or other information, FDA has classified the following indications as lacking substantial evidence of effectiveness as a fixed combination. Dimetapp Extentabs are indicated for symptomatic relief of allergic manifestations of upper respiratory illnesses such as the common cold, seasonal allergies, sinusitis, rhinitis, conjunctivitis and otitis. In these cases it quickly reduces inflammatory edema, nasal congestion and excessive upper respiratory secretions, thereby affording relief from nasal stuffiness and postnasal drip.

CONTRAINDICATIONS: Hypersensitivity to antihistamines of the same chemical class. Dimetapp Extentabs are contraindicated during pregnancy and in children under 12 years of age. Because of its drying and thickening effect on the lower

respiratory secretions, Dimetapp is not recommended in the treatment of bronchial asthma. Also, Dimetapp Extentabs are contraindicated in concurrent MAO inhibitor therapy.

WARNINGS: *Use in children:* In infants and children particularly, antihistamines in overdosage may produce convulsions and death.

PRECAUTIONS: Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. Until the patient's response has been determined, he should be cautioned against engaging in operations requiring alertness such as driving an automobile, operating machinery, etc. Patients receiving antihista-

mines should be warned against possible additive effects with CNS depressants such as alcohol, hypnotics, sedatives, tranquilizers, etc.

ADVERSE REACTIONS: Adverse reactions to Dimetapp Extentabs may include hypersensitivity reactions such as rash, urticaria, leukopenia, agranulocytosis, and thrombocytopenia; drowsiness, lassitude, giddiness, dryness of the mucous membranes, tightness of the chest, thickening of bronchial secretions, urinary frequency and dysuria, palpitation, hypotension/hypertension, headache, faintness, dizziness, tinnitus, incoordination, visual disturbances, mydriasis, CNS-depressant and (less often) stimulant effect, anorexia, nausea, vomiting, diarrhea, constipation, and epigastric distress.

HOW SUPPLIED: Light blue Extentabs in bottles of 100 and 500.

Dimetapp Extentabs®

Dimetane® (brompheniramine maleate), 12 mg.; phenylephrine HCl, 15 mg.; phenylpropanolamine HCl, 15 mg.

A-H-ROBINS

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when pain goes on... and on... and on—



For the patient with a terminal illness, PAIN past, present, and future can dominate his thoughts until it becomes almost an obsession. The more he is aware of the pain he is now experiencing, the more difficult it is to erase his memory of yesterday's pain, and to allay his fearful anticipation of tomorrow's pain.

Surely the last thing this patient needs is an analgesic containing caffeine to stimulate the senses and heighten pain awareness. A far more logical choice is Phenaphen with Codeine. The sensible formula provides $\frac{1}{4}$ grain of phenobarbital to take the nervous "edge" off, so the rest of the formula can help control the pain more effectively. Don't you agree, Doctor, that psychic distress is an important factor in most of your terminal and long-term convalescent patients?

the analgesic formula that calms instead of caffeinates

Phenaphen[®] with Codeine

Phenaphen with Codeine No. 2, 3, or 4 contains: Phenobarbital ($\frac{1}{4}$ gr.), 162 mg (warning: may be habit forming); Aspirin ($2\frac{1}{2}$ gr.), 162.0 mg; Phenacetin (3 gr.), 194.0 mg; Codeine phosphate, $\frac{1}{4}$ gr (No. 2), $\frac{1}{2}$ gr (No. 3) or 1 gr (No. 4) (warning: may be habit forming).

Indications: Provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products, excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.

Ⓒ Phenaphen with Codeine is now classified in Schedule III, Controlled Substances Act of 1970. Available on written or oral prescription and may be refilled 5 times within 6 months, unless restricted by state law.

A. H. Robins Company, Richmond, Va. **A-H-ROBINS**

News, Notes and Announcements

Yellow Fever Immunization Clinic

The Yellow Fever Immunization Clinic for civilians is now being held between 10:00 and 11:00 a.m. every Friday at the U.S. Public Health Service Outpatient Clinic, 331 Veranda Street, Portland, Maine 04103.

No appointment is necessary, however, it is strongly recommended that individuals contact the Clinic regarding other live virus immunizations — smallpox, polio, yellow fever — which must be given within the same 24-hour period, or, (which) must be given 30 days apart. The telephone number is (207) 775-3131, Ext. 210, and Mrs. Ethel Kilbride, R.N. will provide consultation and updated recommendations for immunization based on the individual's itinerary.

American-German Postgraduate Congress

The First American-German Postgraduate Medical Congress will take place between December 26, 1975 and January 9, 1976 at the Holiday Inn in Nassau followed by a Caribbean cruise. Fifteen qualified University Professors from the United States and Germany, all bilingual, will participate in teaching seminars recommended for practicing physicians, internists, cardiologists, family physicians.

Further details may be obtained by writing to: S. Heyden, M.D., Department of Community Health Sciences, Duke University Medical Center, Durham, North Carolina 27710.

Sixth Annual Aspen Radiology Conference

The sixth annual Aspen Radiology Conference will be held March 1st-5th, 1976 at the Aspen Institute for Humanistic Studies, Aspen, Colorado. The Conference is designed for physicians and scientists interested in diagnostic radiology, nuclear medicine and radiation therapy and will explore the impact of clinical and technological advances on radiologic practice.

The topics for discussions will include advances in cardiovascular, gastrointestinal, bone and neuroradiology involving a tri-radiological approach. Each morning will survey the advances in a single radiology subdivision as a refresher course with independent parallel diagnostic, nuclear medicine and therapy sessions. Instructive cases, illustrating these topics and previewed by the audience, will be presented for open discussion in the afternoons.

Further information may be obtained from Emanuel Salzman, M.D., Conference Chairman, Division of Radiology, Beth Israel Hospital, Denver, Colorado 80204.

U.S.-Canadian Division International Academy of Pathology

The 65th Annual Meeting will be held at the Sheraton-Boston Hotel in Boston, Massachusetts, from Tuesday evening 23 March through Saturday 27 March 1976. The annual Maude Abbott lecture entitled "Melanoma: Its Histogenesis and Spontaneous Regression" will be delivered on Wednesday 24 March by Dr. V. J. McGovern, Director, Fairfax Institute of Pathology, Royal Prince Alfred Hospital, Camperdown, Australia.

Eighty scientific papers, 6 pathology specialty conferences, 47 Short Courses, a special seminar honoring Dr. William M. Shelley "Carcinoma of the Breast," a special course on Immunofluorescence in Diagnostic Pathology, a special course on Electron Microscopy, and the Long Course on Inflammatory and Neoplastic Disease of the Gastrointestinal Tract directed by Dr. John H. Yardley and Dr. Basil C. Morson will be given during the meeting.

Further information about the meeting may be obtained from

Dr. Leland D. Stoddard, Secretary-Treasurer, U.S.-Canadian Division, International Academy of Pathology, Department of Pathology, Medical College of Georgia, Augusta, Georgia 30902. Telephone (404) 724-2973.

Information about Short Courses, the IF Course to be given Friday 26 March, the EM Course Friday 26 March and Saturday 27 March 1976, and the Long Course may be obtained from Mrs. J. Preston, IAP Registrar, Armed Forces Institute of Pathology, Room 4090, Washington, D.C. 20306. Telephone (202) 576-2969.

Concise Clinical Neurology Review

The CLINICAL NEUROLOGY INFORMATION CENTER, which is largely supported by the National Institute of Neurological and Communicative Diseases and Stroke (NIH), publishes a biweekly review of articles of interest to the clinical "neuroscientist," appropriately named the "Concise Clinical Neurology Review (CCNR)." In 1975-76 alone, approximately 10,400 articles will be reviewed. Four thousand of these will be presented as "terse conclusions," i.e., a single sentence summarizing the essence of the article. The remaining 6,400 will be presented as references only. The review includes articles published in over 850 regularly recurring journals, over half of which are not later than 3 to 4 weeks after their appearance in the journal. Neuroscientists from many foreign countries as well as the United States and Canada find that the Concise Clinical Neurology Review gives them a comprehensive overview of the vast amount of current information applicable to their field of interest, in an easy to read format.

A two-volume subscription with 13 issues per volume is available at \$15.00 U.S. (\$12.50 U.S. for house officers, students and fellows). Requests for subscription forms, a sample copy or more information can be obtained by writing to: Clinical Neurology Information Center, University of Nebraska Medical Center, 42nd and Dewey Avenue, Omaha, Nebraska 68105, U.S.

11 From Maine Inducted Into Surgeon College

Eleven Maine doctors have been inducted into the American College of Surgeons.

Members must have acquired education and advanced training in general surgery or one of 11 specialties recognized by the college and must give evidence of ethical practice and good character.

Recently inducted in San Francisco were: Robert M. Knowles and Jean J. Labelle, both of Portland; John Zerner and John N. Burke, both of South Portland; Teodoro C. Dela Cruz, of Augusta; H. Richard Hornberger and Tatsuo Watanabe, both of Waterville; John W. Wickenden, of Rockland; Adwaita K. Ganguli, of Rumford; and Charles E. Dixon and Philip R. Kimball, both of Bangor.

Hornberger of Waterville wrote the popular "M-A-S-H" books under the name Richard Hooker.

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County Society Notes

York

The May meeting of the York County Medical Society was held on May 14, 1975 at the Webber Hospital in Biddeford, Maine. The format of this meeting consisted of a Social Hour from 6:30 p.m. to 7:30 p.m., with the dinner, speaker and business meeting to follow.

The featured speaker of the evening, who followed a delicious steak dinner, was Thomas Cathcart, Vice-President of Provider and Public Relations, Blue Cross/Blue Shield, Portland, Maine. His subject was, "Newer Rules and Regulations and Other Aspects of Blue Cross/Blue Shield of Interest and Importance to the Physicians." He was introduced by the President, Dr. Carl E. Richards. A very interesting dissertation was given and a lively discussion followed replete with questions and answers. Following the completion of his talk, Miss Laura P. Franciose and Donald Thompson, members of Blue Cross/Blue Shield administration, were introduced.

After this talk, President Richards called the business meeting to order over which he presided. The minutes of the last meeting were read and approved in the interest of time. There was no old or new business.

The following announcements were made:

1. The Annual Meeting of the Maine Medical Association will be held at the Treadway-Samoset Resort, Rockport, Maine on June 14-17, 1975.

2. The next meeting of the York County Medical Society will be held on October 8, 1975 at the York Hospital, York Village, Maine. The Committee in charge of arrangements for this meeting is Drs. Leigh and Hazzard.

A report was given by Dr. Richards on the Maine Medical Association Interim Meeting of the House of Delegates held April 12, 1975 at the Thayer Hospital, Waterville, Maine. It was extremely long and very informative. Included in this presentation were matters concerning the budget and the resolution of the Cumberland County Medical Society concerning the re-proportion of the representation of the membership of the Committee on Health Care Financing.

He also mentioned the new Health Care Program in Maine as discussed by Dr. Chatterjee and the Blue Cross/Blue Shield representative. It was voted by the House of Delegates, on recommendation of the Executive Committee that the State of Maine be designated as one district. Under the Bylaw Amendments, there was one item of importance which involved the selection of one member to be nominated by each county society before February 1, 1976 to the Executive Committee. He also reported that Robert Rules of Order, newly revised, will now be used to conduct the meetings of the Association. The report of Dr. Robert McAfee, Delegate to the American Medical Association, was given and he stated that no resolutions from the New England Group would be presented this year. Major issues that would be discussed at the American Medical Association convention in June concerned malpractice, PSRO, and the American Medical Association's financial status.

The next item in his discussion concerned a resolution from the York County Medical Society asking the Maine Medical Association to issue a legislative newsletter at appropriate intervals to keep its members informed of State and Federal legislation that may affect the practice of medicine in this State. This was considered too costly and as Dr. Richards mentioned, one can get all this information from the Portland Press Herald every morning. This was extensively discussed. He also brought out the need for a continuation of *The Journal of the Maine Medical Association*. Mention was also made of a Committee of the Maine Medical Association that is going to survey every hospital in the State setting up educational programs for the doctors and also that continued education will be mandatory. A newly proposed medical school for Maine was another item of discussion and the history of such a medical school in Maine was also

presented. Dr. Madigan, President of the Maine Medical Association, indicated the need for a bargaining union in the State. A program for Hemophiliacs was okayed and the malpractice problem was also brought up by him. The proposed increase in dues was discussed and also the reason for its need. One county medical society, namely Androscoggin, was against it. This concluded Dr. Richards' remarks of the meeting of the House of Delegates.

After this, the county society voted in favor of an increase in dues of the Maine Medical Association not to exceed \$50.00. At this time, the Health Mobile in Waterboro was also discussed.

There were 22 members and 5 guests present. The meeting adjourned in a note of harmony and complete accord.

MELVIN BACON, M.D., *Secretary*

Penobscot

The annual meeting of the Penobscot County Medical Society was held on May 20, 1975 at the Tarratine Club in Bangor, Maine.

The minutes of the April 1975 meeting were approved as read.

The following communications were received and read to the membership:

1. A letter from Governor James Longley acknowledging receipt of our communication to him expressing our support of Public Law 93-641 and offering our assistance to him in carrying out this mandate.

2. A letter from Senator Bennett Katz acknowledging our communication to him which informed him of the Society's support for the Medical School of Maine under the university system.

3. A letter received from Richard Nellson, President of the Maine Blue Cross and Blue Shield, requesting nominations from our Society for consideration for the Blue Cross and Blue Shield Award for Outstanding Contribution to Improve Delivery of Health Care and Control of Health Care Costs for the People of Maine.

4. A letter of notification from the Secretary of Health, Education, and Welfare which called for objections from any physician who chose not to consider the State PSRO organization as their rightful representative in PSRO activities.

Under old business, Dr. John J. Pearson requested a progress report on the Medical School of Maine. Dr. Robert Coon addressed his comments to the question and described the movement of the Medical School Bill through the legislative process.

Dr. Edward C. Porter made a motion, and it was seconded and passed, that the Penobscot County Medical Society propose a resolution to the Maine Medical Association and its House of Delegates in support of the American Medical Association's recommendation with regard to medical malpractice.

Under new business, applications were received from Drs. Katherine Lane and Paul M. Beach. Both applicants were unanimously approved into membership of the Society.

The annual election of officers of the Society was then carried out. Dr. Benjamin L. Shapero, Chairman of the Nominating Committee, presented the following slate of officers for the coming year:

President: Dr. Thornton W. Merriam, Jr., Bangor
President-elect: Dr. John A. Woodcock, Bangor
Secretary: Dr. Philip G. Hunter, Bangor
Treasurer: Dr. David S. Beebe, Bangor
Counselor for three years: Dr. William M. Blackwell, Milinocket

By secret ballot, the nominees as presented by the Nominating Committee were unanimously approved.

The nominees for delegate and alternate delegate to the House of Delegates of the Maine Medical Association were presented.

These included the following:

Delegates: Drs. Robert P. Andrews, Francis I. Kittredge, John A. Ordway, Lewis E. Phillips and Leonardo Leonidas, all of Bangor. Alternates: Drs. David S. Beebe, Jack N. Meltzer, Roy S. Patten, James Curtis, all of Bangor and Dr. John J. Pearson, Old Town.

The scientific portion of the meeting featured a presentation by Alexander Marble, M.D., Joslin Clinic, Boston, Massachusetts, titled "Present Status of Oral Anti-Diabetic Agents." Dr. Marble presented data obtained through the diabetic population at the Joslin Clinic in which oral anti-diabetic agents were compared with insulin and diet alone. He contrasted this data to previously published data regarding the efficacy and potential dangers of the oral anti-diabetic agents. Following this interesting presentation, a question and answer session followed.

As there was no further business, the meeting was adjourned.

PHILIP G. HUNTER, M.D., *Secretary*

Kennebec

The Kennebec County Medical Association met on September 18, 1975 at The Holiday Inn in Augusta, Maine. Forty-one members and guests were present. Following a cocktail hour and a very nice dinner, the President, Dr. Joseph J. Hiebel called the meeting to order at approximately 8:00 p.m.

The first item of business was reading the applications of Drs. Nancy Coyne and Robert Day for membership in the Association. The transfer of Dr. Daniel Storer from the Cumberland County Medical Society was made known and the resignations of Drs. Ralph G. Bennett, Jr. and James C. Wren. Dr. Wren has been transferred to affiliate status rather than actually resigning.

Communications were read from a Citizens Commission on Human Rights. A letter from the AMA regarding AMA dues was read and a letter from HEW regarding PSRO designation of PTO was read. Dr. Hiebel then introduced Mr. John Fickett of the Department of Health and Welfare who had been asked to clarify a point regarding physicians' signatures on Medicaid billing. Mr. Fickett explained to the Association why this regulation had been changed, mentioning the fact that it was acceptable for a member of the physician's staff to sign. It just needed to be a designated signature rather than a facsimile and then analyzed some of the problems that the Department of Health & Welfare face in administering the Medicaid program. Following this, the problem of the bylaws of the County Association were discussed. Dr. Chamberlin mentioned that Dr. Hanley had available a set of model County bylaws and we will attempt to obtain them.

The final item of business was a very nice discussion by Dr. Chamberlin of the activities of the Maine Medical Association Executive Committee over the summer. Dr. Chamberlain presented a brief list of the agenda facing the Maine Medical Association Executive Committee which consisted of some thirty-three items, several of which were of considerable interest to members of the County Association. None of these were discussed at any great length. The members of the Association voiced great appreciation for this presentation and were in general approval of the direction of the meeting of the County Association taking a socio-economic and political turn.

The Kennebec County Medical Association met at the Silent Woman Restaurant in Waterville, Maine on October 16, 1975, with thirty-seven members and two guests present. Following a very nice meal, Dr. Joseph J. Hiebel, the President, called the meeting to order about 8:30 p.m.

Business which was conducted included the vote on the applications of Drs. Nancy M. Coyne and Robert B. Day who were both elected to membership. The application of Dr. Martin Vickers, Jr. was read and will be voted upon at the next meeting. There being no other business, Dr. Hiebel introduced the speakers of the evening who were John J. Casey, President and Miss Mary Rose Godfrey, of the New England Physicians Advisory Service. Mr. Casey discussed the new Pension Reform Act, in

the setting of the history of the Keogh Plan and Professional Corporation. He outlined the various ramifications of these plans as they affect physicians. Miss Godfrey mentioned several tax tips. The presentation was well received by the members and the meeting was adjourned at 10:00 p.m.

O. THOMAS FEAGIN, M.D., *Secretary*

Cumberland

The Executive Committee of the Cumberland County Medical Society met at the Mercy Hospital in Portland, Maine on August 12, 1975.

Members present: Drs. Robert E. McAfee, President; Walter B. Goldfarb, Vice-President; Wesley J. English, Secretary-Treasurer; and Harry A. Bliss.

1. Dr. McAfee mentioned we have been remiss in failing to invite Dr. Stanley Sylvester, the immediate past president of the CCMS, to our meetings. The Secretary will write a letter of apology and invite him to future meetings.

2. Applications for membership — First Readings:

1. Dr. James O. Pringle
2. Dr. Walter Christie
3. Dr. Keith N. Megathlin

Application in Transfer:

1. Dr. L. Reed Altemus
- Secretary instructed to inform Dr. Altemus that he is accepted in transfer.

3. Communications:

- A. Letter concerning "Swimmers Itch" from the Portland Water District. Secretary to discuss the information with Dr. Hallett — possibly copies of a reprint should be circulated to Pediatricians.
- B. AMA Public Affairs Memo regarding separate specialty listing in telephone company yellow pages to be offered by American Tel and Tel. The matter was tabled until further directives arrive from the AMA.
- C. Letter from Patricia Bergeron concerning move of Dr. Kirk K. Barnes to Rhode Island without resigning his membership in the Maine Medical Association. Secretary to check correspondence to see if a letter of resignation has been received.
4. Reports from Dr. McAfee:
 - A. Committee assignments discussed. They will be finalized soon by Dr. McAfee.
 - B. Education Foundation Report — A total of \$50,000 awarded to 49 applicants.
 - C. Medical Liability Commission — note is made of latest move to bypass the statute of limitations by filing medical injury suit without proving malpractice.
 - D. Medical School for Maine — Recent proposals by the committee (Friends of Maine Medical School) to obtain sufficient signatures for referendum discussed. No official action taken.
5. The meeting adjourned at 6:45 p.m.

The Executive Committee of the Cumberland County Medical Society met at the Mercy Hospital in Portland, Maine on September 9, 1975.

Members present: Drs. Robert E. McAfee, President; Walter B. Goldfarb, Vice-President; Wesley J. English, Secretary-Treasurer; Harry A. Bliss; Ronald J. Carroll; Douglas R. Hill; Stanley Sylvester; and Philip G. Whitney. Guest present: Dr. Stuart W. McGuire.

1. Dr. McGuire reported on preparations for the Outing at the Homewood Inn on September 18, 1975.

2. Diabetes Detection — Letter received from Pat Bergeron requesting name of Diabetes Detection Officer for CCMS Dr. Saunders, although he has served in the past, is unwilling to be the Chairman, and he has raised some valid questions as to whether or not such a committee should exist under the CCMS. He pointed out the work of the Pine Tree Diabetes Association and feels that this Association (of which he is a member) does a

better job of supporting Diabetes Week and Diabetes Detection than the local committee of the State Medical Association. He is, however, willing to support anyone chosen by the Executive Committee to serve as the Chairman for the local committee of the M.M.A. Dr. Hotelling and Dr. Bigos were suggested as possible candidates for the Chairmanship of the local Committee. Dr. McAfee will review a communication from Dr. Saunders to Dr. Sylvester regarding this matter before taking any further action.

3. Annual Member-Spouse Night at Union Mutual — Problem exists in that liquor cannot be sold at Union Mutual for profit. Decision made to have open bar. The members will be charged a fee for their wife's dinner, as has been the custom in the past. Dr. McAfee has suggested inviting Mrs. Muskie to be the guest

speaker, to be accompanied by her husband, who was voted the father of the year recently.

4. PSRO — Some informational material was discussed on PSRO. No decision on this material was required.

5. Applications for Membership — Second Readings: Drs. James O. Pringle, Walter Christie and Keith N. Megathlin. All were approved for membership.

6. Letter received from Lieutenant Blake of the U.S. Air Force — Pease Air Force Base. He wants to address the medical society concerning career opportunities for physicians in the Air Force. Executive Committee not favorably disposed and secretary will notify Lieutenant Blake of negative reaction.

7. The meeting adjourned at 7:00 p.m.

WESLEY J. ENGLISH, M.D., *Secretary*

Letters to the Editor

To the Editor:

RE: EMERGENCY ROOM PHYSICIANS

An increasing number of hospitals are seeking physicians to work in their emergency rooms on a full-time basis. This plan has much to commend it. Many emergency room physicians are properly trained for the job and can cope in a highly satisfactory manner with the varied problems that confront them. On the other hand, the plan is doomed to failure if the physician is recruited from the ranks of those who have had a substandard record of performance and is accepting the new position only as an escape from his previous practice.

To upgrade the care of patients in emergency rooms, I should like to make the following recommendations:

First, only the most qualified physicians should be accepted. It is far better not to have a full-time physician than to have one who is inadequately trained and poorly motivated. He can do more harm than good.

Second, if the qualified physician has not had previous training in handling the diverse problems of the emergency room, he should be required to attend an approved Emergency Room Seminar at the start of his appointment.

Third, it should be mandatory that he spend at least one week annually to attend courses geared to his needs. Because of the new developments in trauma, fluid and electrolyte balance and in the treatment of shock of all types, the importance of continuing education in these fields cannot be overemphasized.

Finally, more teaching hospitals should initiate well-planned seminars in emergency medicine to satisfy the growing demand for continuing education as stated above. Implementation of these proposals should enhance the quality of care of the extremely sick patient and prove to be a gratifying experience for the physician as well as his patient.

ALFRED HURWITZ, M.D.
10 Abenaki Road
Augusta, Maine 04330

To the Editor:

RE: CHANGE IN DISCLOSURE POLICY

The Privacy Act of 1974 effective September 27, 1975 has changed the disclosure policy regarding medical evidence. Individuals will now be able to *personally* obtain, for *any* purpose, medical reports contained in their files which were furnished by treating physicians, consultative examiners and other medical sources. The only reason for not disclosing medical evidence directly to the individual involved would be a decision that the evidence would have an adverse effect on him. If this judgment is made, a medical representative, through whom the record may be disclosed, would be designated. Because of this policy change, we wish to ask that only objective reports be submitted.

Statements regarding malingering or judgments as to disability should be excluded. This type of reporting is in the current trend to which we are all becoming accustomed of revealing only objective medical data.

Questions regarding this policy may be directed to:

Lorrimer M. Schmidt, M.D.	Chief Medical Consultant	289-2741
Floyd B. Goffin, M.D.	Medical Consultant	289-2741
H. Douglas Holloway	Director	289-2741
Ann D. DeWitt	Assistant Director	289-2741

We thank you for your past and anticipated cooperation.

H. DOUGLAS HOLLOWAY, DIRECTOR
Disability Determination Services
State of Maine, Department of Health
and Welfare
Augusta, Maine 04330

To the Editor:

Here are some views on marijuana from a longtime physician and psychiatrist:

You have only one mind; why let it "go to pot"? Your brain is your most precious possession. Guard it well. It is irreplaceable. Smoking marijuana often leads to slavery to heroin and other more feared hard drugs and is never a wise experiment.

I have practiced medicine for a long time. I have learned much about the drug addict that I did not learn in medical school, though I graduated from one of America's best medical schools, Washington University Medical School of St. Louis. Though well versed in drugs, reputable physicians never prescribe marijuana. It does nobody any good.

I firmly believe that the drug Marijuana *should be wiped off the face of the earth*. It should be avoided like the bubonic plague. Today it does the world more harm than the bubonic plague, TBC, and polio combined.

Marijuana is a *much more serious drug menace* than is realized by most science writers, or by anyone who has not been *incessantly frustrated* by marijuana brain damaged drug addicts whom he as an M.D. was trying to help eradicate their tenacious vicious habit. The victims want substitute narcotics, almost none really want to stop using all narcotics. Almost none use marijuana only. The pusher and underworld see to that.

Since 1931, I have read most of what has been written by reliable medical men on marijuana, and I have been associated with this awesome problem as a psychiatrist through trying to help the distraught victims who unwillingly let themselves be "hooked" on this exceedingly dangerous drug before they woke up, or even believed it is often the direct road to the prison of an insane asylum.

ADRIAN H. SCOLTEN, M.D.
Carolina Village
Hendersonville, N.C. 28739

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MDS



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The following Specialties, including Family Practice, are recognized by the American Medical Association:

A	Allergy (sub-specialty of Internal Medicine)	OPH	Ophthalmology
ANES	Anesthesiology	ORS	Orthopedic Surgery
AM	Aerospace Medicine (special field of Preventive Medicine)	OTO	Otolaryngology
CD	Cardiovascular Disease (sub-specialty of Internal Medicine)	PATH	Pathology
CHP	Child Psychiatry (sub-specialty of Psychiatry)	PD	Pediatrics
CRS	Colon and Rectal Surgery	PDA	Pediatric Allergy (sub-specialty of Pediatrics)
D	Dermatology	PDC	Pediatric Cardiology (sub-specialty of Pediatrics)
DR	Diagnostic Roentgenology (special field of Radiology)	PMR	Physical Medicine and Rehabilitation
FOP	Forensic Pathology (special field of Pathology)	PS	Plastic Surgery
FP	Family Practice	P	Psychiatry
GE	Gastroenterology (sub-specialty of Internal Medicine)	PH	Public Health (special field of Preventive Medicine)
GPM	General Preventive Medicine (special field of Preventive Medicine)	PUD	Pulmonary Diseases (sub-specialty of Internal Medicine)
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NS	Neurological Surgery	TS	Thoracic Surgery
N	Neurology	U	Urology
OBG	Obstetrics and Gynecology	00	Unspecified (retired, not in practice, no specialty reported)
OM	Occupational Medicine (special field of Preventive Medicine)	99	Other

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The figures in parentheses refer to County Societies as follows: (1) Androscoggin, (2) Aroostook, (3) Cumberland, (4) Franklin, (5) Hancock, (6) Kennebec, (7) Knox, (8) Lincoln-Sagadahoc, (9) Oxford, (10) Penobscot, (11) Piscataquis, (12) Somerset, (13) Waldo, (14) Washington, (15) York.

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 LaCasce, Joseph H., 50 Union St., Ellsworth 04605 (5)
 LaFlamme, Paul J., 106 Russell St., Lewiston 04240 (1)
 LaFond, Robert S., 258 Main St., Saco 04072 (15)
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 Lape, C. Philip, R.F.D. No. 1, Orrs Island 04066 (3)
 Lapirow, Harry, 99 Main St., Kennebunk 04043 (15)
 Lappin, John J., 171 State St., Portland 04101 (3)
 Larned, Frederick S., 155 Spurwink Ave., Cape Elizabeth 04107 (3)
 Larson, Karl V., East Machias 04630 (14)
 Lathbury, Vincent T., Medical Arts Building, Rockland 04841 (7)
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 Leigh, Kenneth E., Brixham Rd., York 03909 (15)
 Leiter, Laban W., 175 Vaughan St., Portland 04102 (3)
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 Lynn, Geraldine, 188 Russell St., Lewiston 04240 (1)

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 MacLeod, Cathel A., 131 Chadwick St., Portland 04102 (3)
 MacVane, William L., Jr., 211 State St., Portland 04101 (3)
 Madigan, John B., Houlton 04730 (2)
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 Marcotte, Gilbert E., 180 Walnut St., Lewiston 04240 (1)
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 Martin, Stuart H., 108 Elm St., Camden 04843 (7)
 Martin, Thomas A., 157 Pine St., Portland 04102 (3)

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 Mason, Peter H., Millinocket Com. Hosp., Millinocket 04462 (10)
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 McMichael, Morton, 73 Deering St., Portland 04101 (3)
 McPhedran, Alexander M., 12 E. Chestnut St., Augusta 04330 (6)
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 Mendros, John G., 394 Sabattus St., Lewiston 04240 (1)
 Mepani, Bhupendra, Wimbleton Ct., Bldg. 112, Apt. #8, Center Rd., Buffalo, N.Y. 14224 (6)
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 Miller, Clark F., Greene 04236 (1)
 Miller, Thor, 752 Main St., Westbrook 04092 (3)
 Milliken, Howard H., R No. 1, Pond Rd., (Manchester), Hallowell 04347 (6)
 Millington, Paul A., 44 Mountain St., Camden 04843 (7)
 Minihan, Patrick T., Naval Rad. Sta., E. Machias 04630 (14)
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 Minton, Paul R., 131 Chadwick St., Portland 04102 (3)
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 Mitchell, Hazen C., Calais 04619 (14)
 Mohlar, Robert G., Doctors Park, 89 Hospital St., Augusta 04330 (6)
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 Moore, Conner M., 372 Main St., Saco 04072 (15)
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 Morton, George L., 180 Park Ave., Portland 04102 (3)
 Mossman, Philip, 489 State St., Bangor 04401 (10)
 Morton, Jeremy R., 321 Brackett St., Portland 04102 (3)
 Moulton, Albert W., Jr., 180 State St., Portland 04101 (3)
 Moulton, Albert W., Sr., 180 State St., Portland 04101 (3)
 Moulton, Gardner N., 5 Grove St., Bangor 04401 (10)
 Moulton, Marion K., West Newfield 04095 (15)
 Mulvihill, John G., 9 Academy St., South Berwick 03908 (15)
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 Mundie, Perley J., 32 North St., Calais 04619 (14)
 Murphy, John J., 84 Portland St., South Berwick 03908 (15)
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 Murtaugh, John F., 7 Palmer St., Ext., Calais 04619 (14)
 Mutty, Richard J., 111 Webster St., Lewiston 04240 (1)
 Nackle, George N., 1 School St., Machias 04654 (14)
 Nadeau, J. Paul, 91 Pine St., Lewiston 04240 (1)
 Nadeau, Lawrence A., 41 Sherbrooke Ave., Lewiston 04240 (1)
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 Nesin, Bourcard, 21 Penobscot Ave., Howland 04448 (10)
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 O'Callaghan, Terence, St. Joseph Hosp., Bangor 04401 (10)
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 O'Kane, Francis R., 200 Spruce St., Millinocket 04462 (10)
 Olmsted, Burton L., 73 Deering St., Portland 04101 (3)
 Onat, Mustafa V., St. George 04857 (7)
 Onion, Daniel K., R.F.D. No. 3, Farmington 04938 (4)
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 Osler, Jay K., 74 Birch St., Bangor 04401 (10)
 O'Sullivan, James V. I., 10 High St., Lewiston 04240 (1)
 O'Sullivan, William B., Box 645, Biddeford 04005 (15)
 Ouellette, Benoit, 1 James St., Fort Kent 04743 (2)
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 Page, Lyman A., 372 Main St., Saco 04072 (15)
 Page, Rosario A., Carrabassett Valley, Kingfield 04947 (2)
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 Pandya, Najib M., 7 Novella St., Lewiston 04240 (1)
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 Patterson, James, Apt. 10D, 45 Eastern Prom., Portland 04101 (3)
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 Pendleton, Arthur D., 3 Green St., Fort Fairfield 04742 (2)
 Pennoyer, Douglass C., 112 Vaughan St., Portland 04102 (3)
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 Peterlein, Walter R., Jr., 75 Main St., Springvale 04083 (15)
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 Shurman, Hans, 10 Spring St., Dexter 04930 (10)
 Siddiqui, Saleem A., 154 High St., Caribou 04736 (2)
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Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor

neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

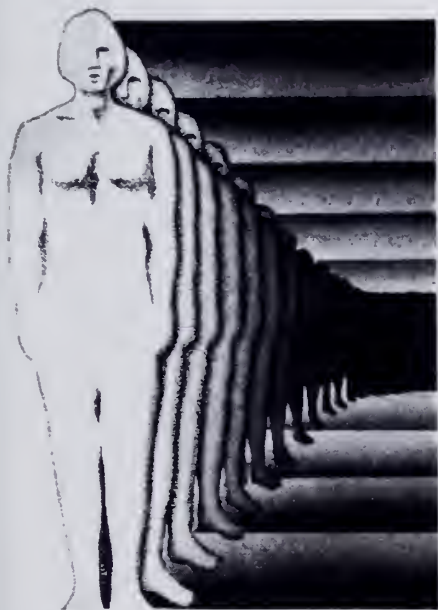
Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive dis-

orders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

PERFORMANCE. IT'S A MATTER OF RECORD.

- an unsurpassed record validated in several thousand clinical papers
- rarely interferes with mental acuity
- wide margin of safety



Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous

occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Usual Daily Dosage: Individualize for maximum beneficial effects. *Oral—Adults:* Mild and moderate anxiety and tension, 5 to 10 mg *t.i.d.* or *q.i.d.*; severe states, 20 or 25 mg *t.i.d.* or *q.i.d.* *Geriatric patients:* 5 mg *b.i.d.* to *q.i.d.* (See Precautions.)

Supplied: Librium® (chlordiazepoxide HCl) Capsules, 5 mg, 10 mg and 25 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Libritabs® (chlordiazepoxide) Tablets, 5 mg, 10 mg and 25 mg—bottles of 100 and 500. With respect to clinical activity, capsules and tablets are indistinguishable.



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LIBRIUM® ^{IV}

chlordiazepoxide HCl/Roche
5 mg, 10 mg, 25 mg capsules

**IN PAINFUL
ACUTE
CYSTITIS***

*nonobstructed;
due to susceptible
organisms



92

RELIEVE THE PAIN WHILE YOU ELIMINATE THE PATHOGENS.

FOR THE PAIN

- ☐ **Early relief of painful symptoms** such as burning and pain associated with urgency and frequency.

FOR THE PATHOGENS

- ☐ **Effective control of susceptible pathogens** such as *E. coli*, *Klebsiella-Aerobacter*, *Staph. au-*

reus, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*.

Appropriate antibacterial therapy: Up to 3 days therapy with Azo Gantrisin 4 to 6 tablets *Stat.*, then 2 tablets *q.i.d.*; then 11 days with Gantrisin (sulfisoxazole) may be considered.

AZO GANTRISIN®

(50 mg phenazopyridine HCl and 0.5 Gm sulfisoxazole)

Before prescribing, please consult complete product information, a summary of which follows.

Indications: In adults, urinary tract infections complicated by pain (primarily cystitis, pyelitis and pyelonephritis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies.

Important Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media for patients already taking sulfonamides. Increasing frequency of resistant organisms currently is a limitation of the usefulness of antibacterial agents including the sulfonamides. Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses, 12 to 15 mg/100 ml is considered optimal for serious infections; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Children below age 12, sulfonamide hypersensitivity, pregnancy at term and during nursing period. Contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with gastrointestinal disturbances, because of phenazopyridine HCl component.

Warnings: Safe use in pregnancy has not been established. Teratogenicity potential has not been thoroughly investigated. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination should be performed frequently during sulfonamide therapy.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* Agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia.

Allergic reactions: Erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis. *C.N.S. reactions:* Headache, periph-

eral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, polyarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Usual adult dosage for acute, painful phase of urinary tract infections is 4 to 6 tablets initially, then 2 tablets four times daily for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment of the infection with Gantrisin (sulfisoxazole) may be considered.

Note: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine soon after ingestion.

How Supplied: Tablets, each containing 0.5 Gm sulfisoxazole and 50 mg phenazopyridine HCl—bottles of 100 and 500.

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